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Modern treatment methods in atopic dermatitis-literature overview

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Abstract

Introduction and aim: Atopic dermatitis (AD) is a chronic inflammatory skin disease. It is characterised by periods of exacerbation and remission of symptoms such as pruritus, dry skin and eczematous lesions with characteristic morphology. The aim of this study is to present the current state of knowledge on new treatments for atopic dermatitis.

Review methods: The review was based on publicly available PubMed and Google Scholar databases from 2020 to 2024 using the following phrases: atopic dermatitis, treatment of atopic dermatitis, diagnosis of atopic dermatitis, epidemiology, biological treatment of atopic dermatitis, JAK inhibitors, stem cells, dermatitis.

Brief description of the state of the art: Atopic dermatitis is a disease whose mechanism of origin is incompletely understood.It involves interactions between genotype, environment, and the immune system, and is largely related to the T-cell response. The main symptom is pruritus and dry skin leading to lichenification or exfoliation of the epidermis, which characterise the chronic form. Diagnosis is confirmed by clinical criteria such as skin lesions characteristic of AD, a family predisposition to allergic disease and a full history and skin tests. Treatment focuses on managing the symptoms associated with the disease and improving the patient's quality of life using mainly corticosteroids, calcineurin inhibitors and antihistamines. Recent studies show positive effects of treatment with biologic drugs, JAK inhibitors, stem cells and provide great hope towards the development of treatments for atopic dermatitis.

Summary: The authors emphasise the need for further research towards the development of promising, innovative treatments for atopic dermatitis in order to significantly improve patients' quality of life.

Keywords: atopic dermatitis, treatment of atopic dermatitis, biological treatment of atopic dermatitis, stem cells, JAK inhibitors.

Introduction

Atopic dermatitis (AD) is a non-infectious inflammatory disease of a chronic or recurrent nature, with periods of remission and exacerbation. The main symptoms are recurrent pruritus and dryness of the skin, and there are typical eczematous lesions with characteristic morphology. In the chronic type of the disease, lichenification or exfoliation of the epidermis appears.[1] In affected individuals, we can observe a greater susceptibility to infection, caused by: decreased IgA secretion, decreased lipid content, deposition of fibrinogen and fibronectin deposits. The disease affects 5-20% of people worldwide, usually begins in childhood (up to 1 year of age in 60% of patients), and may be influenced by genetic background, immunological disorders, epidermal barrier defect, environmental factors, psychosomatic factors.

The pathogenesis of the disease is very complex and still not fully understood.[2,3] The pathogenesis of AD involves interactions between genotype, environment and the immune system, particularly the response of T cells, mainly T-helper 2 (Th2) cells. The induction of inflammation by these cells, as well as increased activity of pro-inflammatory cytokines such as interleukin 4 (IL-4), IL-5 and IL-13, play a key role in the pathogenesis of the disease.[4]

The diagnosis of AD is based on a complete history, evaluation of clinical symptoms and skin tests, including allergens and monitoring of skin barrier function. The basic diagnostic criteria are chronic dermatitis with marked dryness, itching, inflammatory changes and a family predisposition to allergic diseases. Exclusion of other skin diseases is also prominent in the diagnosis.[5] The aim of the study was to present the current state of knowledge on new treatments for atopic dermatitis.

Review methods

The review was based on publicly available PubMed and Google Scholar databases from 2020 to 2024 using the following phrases: atopic dermatitis, atopic dermatitis treatment, atopic dermatitis diagnosis, epidemiology, atopic dermatitis biologic treatment, JAK inhibitors, stem cells, dermatitis.

Treatment

Treatment of atopic dermatitis focuses on relieving symptoms, improving the patient's quality of life and controlling chronic inflammation. Pharmacological treatment mainly includes corticosteroids, calcineurin inhibitors, antihistamines and moisturizers. Corticosteroids are effective in reducing inflammation, but their long-term use is associated with the risk of side effects, such as skin atrophy.Treatment also includes preparations aimed at restoring the skin barrier, such as emollients, which reduce skin dryness and improve skin barrier function.[5] In refractory cases, systemic therapies are used, including immunosuppressants such as cyclosporine, methotrexate, as well as treatment with azatiporine.[6,7]

The importance of innovative treatments has been increasing in recent years. M. Durno et al. in their work on patient preferences in choosing treatment for atopic dermatitis identify attributes that determine the value of treatment for the doctor and the patient. Current research findings can have a significant impact on the doctor's and patient's choice of innovative forms of treatment.[8] In the following article, we will try to discuss the latest aspects of AD treatment.

Biological drugs

Modern approaches to treating AD include the use of biologic therapies that target specific inflammatory mechanisms in the patient's body.

Dupilumab

It is the first approved biologic drug for the treatment of AD. It acts as an IL-4Rα inhibitor, blocking IL-4 and IL-13 cytokine signaling, which are responsible for most of the disease's symptoms. Studies have shown that dupilumab is effective in treating AD in both children and adults with moderate to severe forms of the disease. The drug significantly reduces inflammatory symptoms and improves patients' quality of life. A prospective 52-week study and a retrospective study by H. Nakajima et al. showed that the formulation, when used according to the treatment regimen, can be used for long-term treatment.[9,10] An additional advantage of dupilumab is its high survival rate, compared to traditional systemic AD treatments. [11] The use of this treatment improves control of upper and lower respiratory tract diseases in patients with chronic sinusitis with nasal polyps and patients with asthma ranging from dying to severe uncontrolled. The development of comorbidities and side effects is observed less frequently during the use of dupilumab than with conventional systemic drugs. [12] A recent cohort study by M. Tayefi et al. indicates a risk of weight gain during dupilumab therapy. The study compared patients taking the IL-4Rα inhibitor and those treated with other systemic medications, and analyzed other factors that may cause weight gain during biologic treatment. The study showed a significant increase in patients' weight over 24 months, but the mechanism that contributes to weight gain is not yet understood.[13]

Biological drugs under study

Tralokinumab is a monoclonal IgG4λ antibody that blocks the interaction of interleukin 13 (IL-13) with its receptors, IL-13Rα1 and IL-13Rα2. The IL-13Rα2 receptor, which has a limited proliferative, full anti-inflammatory effect, acts as a "decoy" utilizing IL-13. The action of tralokinumab prevents IL-13 signaling through the heterodimeric IL-4Rα/IL-13Rα1 receptor (type 2 receptor), but may also interfere with the regulatory function of IL-13Rα2.

Lebrikizumab is a biologic drug that effluxes IL-13, blocking its action by eliminating its association with receptors (IL-4Rα/IL-13Rα1) and transferring application in the cell. However, this does not involve the association of IL-13 with another receptor, IL-13Rα2. To date, the effects of lebrikizumab have not been directly compared with tralokinumab.

Available published clinical and preclinical studies between 2006 and 2016 on the use of the above-mentioned drugs have not shown serious adverse effects such as cardiovascular events, infections, malignancies.

Therapy with these biologic drugs in AD, although still requiring long-term safety studies, can be said to be generally effective and safe. However, the individual benefits of these formulations and their clinical utility have not been determined, as there are differences such as mechanistic targets, bioavailability, half-life or dosing frequency that may affect clinical experience. [14]

JAK inhibitors

Janus kinase inhibitors (JAKi) represent a new class of drugs for the treatment of atopic dermatitis. Currently approved by the US Food and Drug Administration are topical JAK inhibitors: tofacitinib, ruxolitinib and oral ones: baricitinib, upadacitinb.[15]

A recent study by E.L. Simpson et al. shows the efficacy of ruxolitinib cream applied for 8 weeks. Improvements were obtained in a number of indicators including pruritus, sleep, skin pain and overall quality of life, which was maintained for 44 weeks of its use as needed.[16]

Topical tofacitinib has undergone a 4-week randomized double-blind phase 2a study. The 2% ointment achieved satisfactory results in the treatment of AD, but side effects such as nasopharyngitis, upper respiratory tract infection are the reason for the lack of research development for this drug.[15]

JAKs, oral such as baricitinib, are drugs that inhibit the activity of JAK kinases, key to cytokinin signaling, leading to modulation of the inflammatory response. JAK inhibitors are particularly important in treating forms of AD that are resistant to traditional therapies. Clinical studies have shown that baricitinib effectively reduces the severity of AD symptoms, including pruritus and skin lesions, while reducing the number of disease exacerbations. [17] During ongoing studies, an acceptable level of safety was found during the drug's use, but continuous monitoring of adverse events occurring during treatment and long-term studies are recommended to better analyze the drug's effectiveness.[18]

Studies using upadacitinib show the drug's effectiveness in both adults and adolescents. The drug shows efficacy in reducing AD symptoms and providing a better quality of life. The formulation has acceptable long-term safety and a low risk of side effects. [19,20]

During the study by J.P. Thyssen et al, a higher rate of safety and long-term efficacy was proven with upadacitinib compared to dupilumab for the treatment of body areas such as the head and neck, trunk and upper and lower extremities.[20]

JAK inhibitors have the advantage of rapid onset of action and the possibility of oral administration, which makes them convenient for patients. However, like other immunosuppressants, JAKs are associated with the risk of side effects, such as infections or changes in blood count, requiring constant monitoring of the patient's condition.[15]

Stem cells

Stem cell treatment in atopic dermatitis is an area of intense research. Stem cells, including dermal stem cells and mesenchymal stem cells, have the potential to regenerate damaged epidermis and modulate the immune response. Preliminary studies suggest that stem cell transplantation may improve skin quality, reduce inflammation and improve skin barrier function in patients with chronic AD.

Although stem cell therapies are still in the research stage, they are showing promising results, especially in the context of treating severe and refractory cases of AD. The ability of these cells to modulate the immune response may contribute to better control of the disease, and learning more about the mechanisms of action of these therapies may contribute to the knowledge of better treatment strategies for this disease entity.

Although mild side effects such as headache, fever and risk of embolism have been associated with this type of treatment, none have been reported during AD therapy.

The clinical studies conducted so far on the use of stem cells are still insufficient. Obtaining information on the choice of dose, method of cell administration requires further studies.[21]

Applications

Innovative treatments for atopic dermatitis, including biologic therapies, JAK inhibitors and stem cells, offer new options for patients with chronic and refractory forms of the disease. Biologic drugs such as dupilumab and tralokinumab represent an important step toward more targeted and effective treatment of AD. JAK inhibitors, such as baricitinib, on the other hand, are a promising alternative for patients who do not respond to other therapies. Stem cell therapies, although still in the research phase, show potential in regenerating the skin and improving skin barrier function. In the future, innovative therapies could significantly improve the quality of life of AD patients and revolutionize the approach to treating this chronic dermatological disease.

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Conflicts of Interest

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