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Development and Treatment of Specific Dermatitis Vaccine

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Abstract. Specific dermatitis (SD), notably atopic dermatitis (AD), represents a prevalent group of chronic inflammatory skin diseases characterized by persistent itching, redness, and scaling, which impair daily activities and diminish quality of life. This review examines the mechanisms and clinical applications of biologic therapies targeting interleukins IL-4 and IL-13, central to AD's inflammatory response. Recent studies on tralokinumab and dupilumab, two monoclonal antibodies, demonstrate marked improvements in the Eczema Area and Severity Index (EASI) and Investigator's Global Assessment (IGA) scores, reflecting reduced inflammation and symptom severity. Despite promising clinical outcomes, challenges remain in treatment frequency, high costs, and limited accessibility, especially in lower-income areas. Future directions include developing therapeutic vaccines to achieve durable immune modulation, reducing reliance on biweekly injections, and exploring biosimilars to enhance global accessibility. A comprehensive, integrative approach addressing dermatological, immunological, and psychological aspects will be crucial for advancing personalized AD management and improving patient outcomes.

Keywords: Specific dermatits, IL-4, IL-13, Treatment of SD.

1. Introduction

Specific dermatitis (SD) is a group of chronic inflammatory skin diseases that are characterized by recurring episodes of inflammation, intense itching, and visible redness on the skin. Among the various types of SD, atopic dermatitis (AD) is the most common form, affecting millions of people worldwide. Patients with AD often experience a range of physical and psychological symptoms that can severely impact their quality of life [1].

Physically, the disease manifests through persistent itching, scaling, and skin lesions, which can disrupt everyday activities such as sleeping, working, or socializing. Over time, chronic inflammation may cause the skin to become dry, cracked, and more susceptible to infections due to a compromised skin barrier [2]. This increases the need for medical intervention to manage both the skin condition and its associated complications.

The psychological impact of SD is equally significant. Patients often struggle with the appearance of the disease, especially when the visible symptoms appear on prominent areas such as the face, neck, or hands. The red, rough patches and constant inflammation can cause embarrassment and social anxiety. Studies have shown that individuals with SD are at a higher risk of developing mental health conditions such as anxiety and depression, with prolonged social isolation and stress compounding the mental health burden [3]. The stigma surrounding visible skin conditions can be particularly detrimental,

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leading to lower self-esteem and difficulties in both personal and professional relationships. As a result, mental health care often becomes a crucial component of the overall treatment for SD patients.

The pathomechanism of SD is complex, involving a combination of genetic predisposition and environmental triggers. A family history of AD significantly increases the likelihood that a child will develop the disease, with studies indicating that if one or both parents have AD, their children are more likely to inherit it [4]. Environmental factors, such as climate, pollution, dietary habits, and exposure to allergens, also play a crucial role in triggering or exacerbating the condition. Additionally, individuals living in urban areas with higher pollution levels tend to have a greater prevalence of SD, highlighting the role of external factors in its pathogenesis [5]. The interaction between genetic and environmental factors can intensify the immune response, resulting in more severe disease progression.

In recent years, advancements in dermatological treatments for SD have focused on modulating the immune system to alleviate the symptoms. Unlike traditional vaccines aimed at preventing infectious diseases, emerging SD vaccines target specific immune pathways to reduce inflammation and abnormal immune responses. A promising area of research has been the focus on interleukin IL-4 and IL-13 pathways, which are central to the allergic inflammation seen in AD. While no therapeutic vaccines have yet been approved, ongoing clinical trials and studies have demonstrated the potential of these targeted approaches. Corresponding inhibitors have already shown efficacy in managing SD symptoms, offering hope for future breakthroughs in treatment strategies aimed at improving the lives of those affected by this chronic disease.

2. Mechanism

Anti-IL-13 monoclonal antibody specifically inhibits the action of IL-13, a cytokine that plays a key role in the immune response in vivo, especially in type 2 immune responses. In patients with atopic dermatitis, overexpression of IL-13 leads to chronic inflammation, impaired skin barrier and increased pruritus [6]. This cytokine not only contributes to the production of other inflammatory mediators, but also causes abnormal functioning of keratinocytes in the skin, leading to disruption of the skin barrier and promoting the production of immunoglobulin E (IgE), which triggers or exacerbates allergic reactions [6]. Anti-IL-13 monoclonal antibody interrupts the signaling pathway mediated by IL-13 by binding to IL-13 and preventing it from binding to the IL-13 receptor on the surface of immune cells and skin cells, thereby interrupting the signaling pathway mediated by IL-13 [6].

Anti-IL-4 monoclonal antibodies specifically inhibit the action of IL-4 [7]. IL-4 is a key cytokine in the Th2-type immune response, promoting IgE production, activating eosinophils, and triggering an inflammatory response, which plays a central role in the pathology of AD [7]. By blocking the interaction of IL-4 and its receptors, the JAK-STAT signaling pathway mediated by it can be inhibited, reducing the release of inflammatory factors and alleviating skin inflammation. Anti-IL-4 monoclonal antibodies effectively block downstream inflammatory signaling by directly binding to IL-4 and preventing the interaction of IL-4 with the IL-4 receptor (IL-4Rα) [7]. In addition, IL-4 receptor antagonists can further attenuate the inflammatory response by competitively binding to IL-4Rα and preventing the two pro-inflammatory factors, IL-4 and IL-13, from acting together [8]. Since IL-4 and IL-13 share the same receptor complex, inhibition of IL-4 also indirectly inhibits the action of IL-13 [8]. Another effective method of inhibition is JAK inhibitors, which directly inhibit the activation of the JAK-STAT signaling pathway, blocking the IL-4-mediated immune response and further reducing the production of inflammatory mediators [7].

3. Case Study

Articles with extant approaches to SD treatment have been browsed, and these research approaches have focused on targeted therapies for the IL-4 and IL-13 pathways. Two important therapeutic approaches are taken up for elaboration in this paper, in both of which two scoring systems, the Eczema Area and Severity Index (EASI) and the Investigator's Global Assessment (IGA), were used for analysis.The EASI total score ranges from 0-72, looking primarily at the affected skin area and the skin's appearance. The EASI score ranges from 0-72 and looks at the area of skin affected and the severity of skin damage,

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with the higher the score the more severe the symptoms, while the IGA is a standardized subjective diagnosis made by the clinician, with a total score ranging from 0-5, again with the higher the score the more severe the symptoms.

3.1. Case Study 1: Tralokinumab Targeting IL-13 in AD Treatment [9]

This study focused on tralokinumab, a monoclonal antibody that specifically neutralizes IL-13. This study was a randomized, double-blind, placebo-controlled clinical trial to minimize bias in the experiment. Participants were selected from 204 patients aged 18 to 75 years old with moderate-to-severe AD, and the study sites were set up in academic dermatology medical centers and hospitals in the United States, Germany, France, and other European countries. Patients were randomly assigned to receive tralokinumab injections at doses of 45, 150, or 300 mg every two weeks in combination with topical glucocorticoid therapy for 12 weeks. Changes in EASI and improvement in IGA scores were observed at the end.

The results showed that patients treated with 300 mg tralokinumab showed a significant reduction in EASI scores, with a mean difference of 24.94 (P=0.01) compared to the placebo group. Meanwhile, 26.7% of patients achieved an IGA score of 0 or 1, significantly better than the 11.8% in the placebo group. In addition, patients experienced a reduction in skin inflammation and pruritus, and the common adverse effect was mild upper respiratory tract infection.

3.2. Case Study 2: Dupilumab targets IL-4 and IL-13 in AD [10]

Dupilumab is a fully humanized monoclonal IgG4 antibody capable of blocking the pathogenesis of atopic dermatitis by inhibiting the IL-4 and IL-13 signaling pathways. This study was also a randomized, double-blind, placebo-controlled study divided into two phases, SOLO1 and SOLO2, and the CHRONOS trial, which evaluated the effects of Dupilumab in combination with topical corticosteroids (TCS). Participants were selected from 1,379 patients with moderate-to-severe AD, aged 18 to 75 years, from North America, Europe and Asia. Patients in each group were randomly assigned to receive 300 mg of Dupilumab injected every two weeks or weekly in conjunction with topical TCS in the CHRONOS trial. The SOLO1 and SOLO2 trials lasted 16 weeks and the CHRONOS trial lasted 52 weeks. The EASI and IGA were used as the primary metrics analyzed in this study, and the Numeric Rating Scale (NRS) and Dermatology Life Quality Index (DLQI) were additionally used as secondary assessments.

The SOLO1 and SOLO2 trials showed significant improvements in both primary and secondary outcomes with Dupilumab. In the SOLO1 trial, 37% of patients receiving weekly Dupilumab injections achieved an IGA score of 0 or 1, compared to only 10% in the placebo group. In addition, 52% of patients receiving weekly Dupilumab achieved an EASI-75 compared to 15% in the placebo group. These results were similarly validated in SOLO2. In the CHRONOS trial, 64% of patients treated with Dupilumab in combination with TCS achieved EASI-75 at week 52, compared to 22% in the placebo group. In addition, patients treated with Dupilumab experienced significantly fewer acute episodes of atopic dermatitis and had more drug-free days of topical hormone therapy.

4. Conclusion

In conclusion, the treatment of specific dermatitis (SD), particularly atopic dermatitis (AD), has seen significant advancements, particularly through the development of biologic therapies targeting cytokines like IL-4 and IL-13. Clinical studies on monoclonal antibodies such as tralokinumab and dupilumab have demonstrated notable efficacy in reducing symptoms of AD, including inflammation, pruritus, and skin lesions. These therapies provide patients with moderate-to-severe AD with new treatment options, showing improvements in both Eczema Area and Severity Index (EASI) and Investigator's Global Assessment (IGA) scores. However, while biologics offer promising results, challenges remain regarding their high cost, frequent injection schedules, and potential side effects, which may limit accessibility for patients without comprehensive health insurance, especially in lower-income regions. The long-term safety of these treatments also requires further investigation to assess the potential risks

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of prolonged immune suppression. Future research directions include the development of therapeutic vaccines that offer more durable immune modulation, reducing the reliance on frequent injections, and efforts to lower the cost of treatment, making these therapies accessible to a broader patient population globally. Additionally, comprehensive reviews that integrate findings from various fields would help clinicians better understand the complex interplay of genetic, environmental, and immunological factors in AD, facilitating more personalized and effective treatments.

5. Discussion

Case studies 1 and 2 provide information on Tralokinumab and Dupilumab in the treatment of moderate-to-severe atopic dermatitis (AD), with the overall aim of providing important support for the efficacy of targeting IL-4 and IL-13 cytokines. Both studies used two internationally standardized tools, the Eczema Area and Severity Index (EASI) and the Investigator's Global Assessment (IGA), to measure clinical improvement. These scoring systems provide a clear, objective framework for quantifying disease severity and monitoring treatment response. In both studies, the randomized, double-blind, placebo-controlled trial design effectively reduced bias and ensured the scientific validity and accuracy of the results. Although these methods and results show promise, there are still some limitations in the studies that need to be further analyzed. For example, the significant improvement in EASI scores and IGA scores with Tralokinumab, while significant, was achieved in a relatively low percentage of patients, 26.7%, who achieved clear skin lesion status (IGA 0 or 1) [9]; in comparison, Dupilumab was 37% in the SOLO1 study and 37% in the CHRONOS study to 64% [10]. This suggests that the efficacy of Dupilumab may be more significant especially in long-term treatment.

A major challenge in the current study is the length of treatment. While the CHRONOS trial showed that Dupilumab's efficacy lasted for more than a year, this efficacy relied on consistent bi-weekly injections [10]. Such a frequent long-term treatment regimen may interfere with patients' self-consciousness about injections, and regular injections are inconvenient for patients' lives. Similarly, Tralokinumab requires injections every two weeks for a 12-week treatment cycle and may be extended depending on patient response [9]. This means that both treatment options are more of a chronic management strategy than a one-time curative approach, making the process of treating AD more complex and variable for patients.

Another key issue is the cost of healthcare. Biologics like Dupilumab and Tralokinumab are costly. The high cost of producing monoclonal antibodies, coupled with frequent injections, further increases the overall cost of treatment. Affording these treatments can be difficult for patients without comprehensive health insurance. Although Dupilumab is considered a breakthrough therapy in the management of AD, its high cost prevents this treatment from being widely used globally, especially in low- and middle-income countries.

Regarding side effects, although the majority of adverse reactions reported in both studies were mild (nasopharyngitis and injection site reactions), a proportion of patients still experience uncomfortable symptoms such as upper respiratory tract infections while being treated with these antibodies [9].Dupilumab has shown to be well-tolerated, but the incidence of conjunctivitis in patients during treatment is high. This can raise patient concerns about the long-term effects of specific side effects [10]. In addition, the long-term suppressive effects of biologics on the immune system are unclear, which makes long-term monitoring and further safety studies necessary.

One of the future research directions is the development of novel vaccines. Therapeutic vaccines for immune dysregulation, especially those targeting the IL-4 and IL-13 pathways, are expected to provide longer-lasting therapeutic effects. Vaccines may reduce patients' reliance on biweekly injections and achieve more durable immune modulation than current biologics. For example, research into how to modulate the function of T cells or other immune cells to reduce overreaction of Th2 cells would be an area of potential.

Another key direction is to reduce the cost of treatment. With advances in biotechnology, particularly the optimization of monoclonal antibody manufacturing techniques, it may be possible in the future to reduce the cost of production of these treatments, thereby making treatments such as Tralokinumab and

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Dupilumab more widely available globally. At the same time, the development of biosimilars (i.e., lower-priced alternatives to biologics) may also significantly reduce the cost of treatments, making these therapies widely available in less-resourced regions.

It is also critical to address safety concerns. Current research suggests that these therapies were safe during the 16- to 52-week trial period, but further follow-up studies are needed in the future to follow patients for many years and assess potential long-term risks. This includes not only immune-related side effects, but also effects on common comorbidities of AD (asthma and allergic rhinitis).

A major shortcoming in the current study is the lack of a comprehensive summary review. Atopic dermatitis is a complex disease involving dermatology, immunology, and mental health. However, existing research tends to be fragmented, focusing more on a specific biologic or treatment and lacking a comprehensive summary of the entire field. An integrative review can combine findings from multiple fields, including dermatology, immunology, and mental health, to provide a clearer overall picture for a comprehensive understanding of atopic dermatitis. Such a comprehensive review would not only help future research to identify current issues, such as the long-term efficacy of biologics or the interplay between genetic and environmental triggers, but would also provide clinicians with more accurate treatment metrics, helping them to develop more personalized treatments and improve long-term outcomes for patients.

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