



Assessment and Management of Atopic Dermatitis in Primary Care Settings

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Article History	Abstract
Received: 06 June 2023 Revised: 05 Sept 2023 Accepted: 18 Nov 2023	<p>An increasingly common chronic inflammatory skin condition is atopic dermatitis (AD). It exhibits severe itching as well as recurring eczematous lesions. New difficulties for treatment selection and approach occur with the expansion of available therapy alternatives for healthcare professionals and patients. The article highlights recent developments in scientific research on atopic dermatitis diagnosis and assessment that have led to the identification of novel therapeutic targets and the development of targeted therapies, both of which have the potential to completely change the way AD is treated, particularly in a primary care setting.</p>
CC License CC-BY-NC-SA 4.0	<p>Keywords: Atopic Dermatitis, Flare, Topical, Corticosteroids, Eczema; Primary Care Setting.</p>

1. Introduction

Atopic dermatitis (AD), also known as "Eczema," is a chronic and recurring pruritic, inflammatory, and eczematous skin condition. The eczematous feature of AD, which presents as erythema, scaling, rusting, and blister formation in addition to serous leakage and rusting, is one of the several dermatological signs that define AD [1]. AD affects over 200 million people globally [2]. The prevalence of AD has significantly grown during the past few decades, especially in high-income countries [3,4]. The first year of life is when it most usually occurs, even though it can begin at any age [5]. AD frequently advances in a chronic, relapsing-remitting way [4]. While many AD sufferers may find resolution or improvement by late childhood, a significant number of people will continue to have flare-ups even after lengthy periods of remission [6].

The multifactorial etiology of AD involves genetic, immunological, and environmental factors. A family history of atopic illnesses has proved a strong predictor of AD, showing the role of genetic factors in the disease's development. Loss-of-function mutations in the filaggrin (FLG) gene, which produce immunologic responses and the emergence of AD, are examples of genetic vulnerability brought on by epidermal barrier failure, which increases epidermal permeability to allergens and pollutants in the environment [7].

The prevalence of AD varies greatly over the world due to geographical, country-specific, age group, and data-collection methodological differences, affecting 0.2% to 36% of the pediatric population (ages 18 years) [8]. This high prevalence emphasizes the significant public health cost that AD imposes on society, together with the high patient/caregiver burden and rising healthcare utilization. Additionally, almost 50% of AD patients receive treatment in a primary care setting, and community-based primary care practices indicate that a significant proportion of their pediatric patients have AD. As a result, pediatricians are crucial in the treatment of AD [9]. Since most cases of AD are mild, general care physicians rather than specialists may be able to handle them. 11% of the issues that General Practice registrars face is skin-related. 12% of them are "dermatitis," which includes AD [10].

In the primary care context, two-thirds of children with mild AD may probably be handled, and primary care physician (PCPs) continue to be crucial in the management of mild AD in kids who are sent to a dermatologist. However, a lot of PCPs, including more than half of pediatricians in the United States (US), recommend dermatologists for even moderate AD. This is perhaps because pediatric PCPs find it difficult to diagnose and treat AD or follow AD guidelines. There are rules for managing AD effectively. Some therapeutic decision-making processes, however, lack useful algorithms or guidelines, which may be perplexing to PCPs. Due to a paucity of dermatologists, particularly those who treat children, accept government-funded insurance, and/or work in rural regions, dependence on subspecialty management of AD is problematic in many nations [11]. Compared to 65% of patients who consulted a pediatrician for AD, 81% of patients who saw a dermatologist received a prescription for topical corticosteroids. In the US, there is only one pediatric dermatologist for every 120,000 kids [11].

As AD is a disease with a high incidence worldwide, a significant economic burden but is most frequently addressed. However, there is a clear need for improved PCP AD management. This review explains the assessments and assesses the effectiveness of treatments targeted at enhancing the management of AD in primary care.

Prevalence

Due to difficulties associated with the disease, such as the absence of reliable diagnostic tests, the scarcity of commonly used biomarkers, and the relapsing nature of the condition, estimates of AD prevalence vary between research. Although there is significant variance between states (9-18%), numerous well-designed US caregiver-centered surveys have indicated prevalence estimates of 11-13% for eczema that has been medically diagnosed. This is consistent with international statistics [12].

A cross-sectional survey research in the US primary care system found that the prevalence of AD was 24% among pediatric patients aged 0–5 years, ranging from 15% of infants under 1 year to 38% of children aged 4-5 years. According to this survey's evaluation of AD severity, the majority of patients had mild or moderate AD (58%) or severe AD (3%), respectively. Asthma and food allergies were two comorbidities that were more common in the AD group than in the non-AD population [13].

Asthma, allergic rhinitis, food allergies, and mental health conditions including attention deficit disorder/attention deficit hyperactivity disorder (ADD/ADHD), autism, and depression have all been linked to AD in previous research [14].

The impact of AD

AD has a severe negative physical, emotional, and financial impact on patients and their families, which lowers both children's and adults' quality of life. Much of this load is driven by the AD itch, which causes pain and poor sleep. Other effects of AD include taunting and shame over the look of the skin, avoiding particular hobbies like sports, and making certain professional decisions [15]. It has also been discovered that the self-reported impact on quality of life is comparable to what families of kids with cystic fibrosis and/or diabetes suffer [16].

AD has a large financial burden on both individual patients and society as a whole. The direct medical expenses of AD (medical services and health goods) were projected to be \$1 billion in the United States in 2004, as were the costs associated with lost productivity at \$619 million and the costs associated with a reduction in quality of life at \$2.6 billion [17]. The prices of over-the-counter drugs, which may be highly expensive for patients and their families, were not included in those estimations. These figures are probably much higher now given the rising frequency of AD and the general rise in health care expenses [18].

Diagnosis of AD

Because there is no good biomarker for AD, the diagnosis is based on clinical presentation. The original *Hanifn and Rajka* [19] diagnostic criteria were modified by the UK Working Party [20] in 1994 and again by the American Academy of Dermatology (AAD) in 2003 in an effort to create and refine a diagnostic tool that is appropriate for clinical practice [21]. According to the AAD recommendations, a clinical diagnosis should be made using the history, morphology, and location of skin lesions, as well as any accompanying clinical signs. Criteria to consider in the diagnosis of patients with AD include essential features such as pruritus and eczema; important features that support an AD diagnosis such as early age of onset, atopy, and xerosis; and associated features suggestive of an AD diagnosis such as atypical vascular responses, keratosis pilaris/pityriasis alba/hyperlinear palms/ichthyosis, ocular/peri [22].

Given the heterogeneous character of the illness, it is significant to emphasize that the differential diagnosis for AD might be vast [22]. The exclusion of conditions like impetigo, scabies, seborrheic dermatitis, contact dermatitis, ichthyoses, cutaneous T-cell lymphoma, psoriasis, photosensitivity dermatoses, immune deficiency diseases, and erythroderma of other causes is required, according to AAD guidelines, for a diagnosis of AD. It might be challenging to rule out illnesses like impetigo and molluscum contagiosum since they may coexist with an individual's AD and perhaps make it worse [23].

Assessment of AD

Identification and assessment of disease severity may be beneficial for differentiating AD, monitoring disease progression, and evaluating treatment effects. Numerous severity indices, such as body surface area, Investigator's Global Assessment (such as the V-IGA, a validated global assessment score), Eczema Area and Severity Index (EASI), SCORAD, and Patient-Oriented Eczema Measure (POEM), can be used to measure the severity or intensity of a disease [24]. The POEM index, a clinically validated patient-derived measure of seven symptoms on a 5-point scale, and an updated version of SCORAD known as the patient-oriented SCORAD index were recently recommended for use in evaluating the severity of atopic dermatitis. This was stated in a consensus statement for the global, multi-professional Harmonizing Outcome Measures for Eczema (HOME) initiative. These tools allow pediatricians to more precisely monitor the progression of their patients' illnesses and modify their treatment plans as necessary [25].

Role of primary care

Primary care clinicians, or PCPs, are in a great position to help both patients and doctors as dependable and accessible members of the healthcare team in the management of AD. Patients with AD may go to a chemist first for over-the-counter medications, making chemists a common entrance point into the healthcare system. Additionally, chemists frequently have built a strong connection with their patients. As a result, they are able to reevaluate their patients' comprehension of their condition and treatment plan as well as promote non-pharmacological interventions and treatment adherence. PCPs have received training in the management of medication-related issues, and they are essential to the continuing optimization and monitoring of the safety, efficacy, drug interactions, and adherence to prescribed AD therapy [26].

Management goals

The main objectives of therapy are to improve Quality of Life, reduce skin inflammation and pruritus, and restore skin barrier function. It is recommended to establish therapeutic objectives for each patient before beginning care. It is advised to employ the Eczema Area and Severity Index (EASI), Physician Global Assessment (PGA), Dermatology Life Quality Index (DLQI), and pruritus Numerical Rating Scale (NRS) in daily practice to set and track the accomplishment of treatment goals and direct therapy.

Management

Daily skin care:

The preservation of the skin barrier with liberal use of emollients and avoidance of aggravating elements are part of general daily skin care for AD. It is becoming more widely accepted that a compromised skin barrier is the main pathogenic component in AD. Moisture can escape from the skin and allergens and irritants can enter the skin due to a damaged skin barrier [26].

Defects in the epidermal barrier, including mutations in the protein filaggrin, can be hereditary, subsequent to inflammation or environmental causes. Applying unscented moisturizers often

throughout the day helps to rehydrate the skin and restore its barrier function. This includes using moisturizers right away after taking a bath or shower [26].

It is impossible to overstate the significance of moisturizer usage in the management of AD given that it has been shown to lower the frequency of AD flares and the requirement for topical corticosteroid (TCS) administration [27]. According to research published in the literature, regular moisturizer usage can reduce the severity of eczema in skin that is currently inflamed and can prolong the time between flare-free episodes. Emollients are described in the literature as a component of several moisturizer products that soften the skin [28].

Different active components, including as occlusive agents, emollients, and humectants, are used in variable concentrations in the formulation of moisturizers. As occlusive emollient moisturizers or humectants, moisturizers come in a variety of forms, including cream, ointment, and lotions. Every moisturizer has a different combination of active substances with varying degrees of hydrophobic and hydrating qualities. Although occlusive emollient ointments are typically better, patients could find their oily texture unattractive on an aesthetic level. Occlusive emollient creams are a good substitute in the situation. For many people, applying creams to open or fissured areas of AD will sting more than using ointments. Since lotions have a larger water-to-oil proportion than creams, they are less effective in the management and prevention of AD [29].

Due to the paucity of current head-to-head trials, the advantage of topical ceramides over other moisturizers is not clearly established. Patients' tastes vary despite these factors, thus the ideal moisturizer is the one that the patient will use frequently and abundantly. There is a chance of unfavorable responses with all moisturizers, including irritating reactions, contact allergies, and folliculitis. Humectants, such as urea, may not be a viable alternative for the patient since they might irritate the afflicted skin. The key to managing AD well is to moisturize and take care of your skin [30].

Basic skin care includes moisturizing as well as identifying and, where possible, avoiding irritants. In general, AD patients have more sensitive skin, and irritants might cause AD to start or worsen in them. One must first identify probable AD triggers through rigorous history gathering in order to minimize aggravating conditions. There are additional recognized physical and chemical irritants that AD patients should usually avoid in addition to these probable patient-specific AD triggers. For optimum hydration, moisturizer application to skin that has been damaged by AD and skin that has not is advised to be done at least twice daily within 3 minutes of bathing [31].

Inflammation and pruritus/AD flare:

The signs and symptoms of AD recur often. While some people have a chronic, actively progressing illness, the majority experience symptoms that fluctuate between different manifestations of active illness and times of remission. Since each AD patient's condition progresses differently, treatment should be customized taking into account both patient (age, adherence) and disease (extent, distribution, acute flare-up or chronic disease) characteristics. The exacerbation of AD symptoms (pruritus, pain, restricting daily activities), the recurrence of previously in remission skin lesions, and the onset of new AD lesions are all indicators of acute AD flares. Management of AD flares emphasizes regular skin care and inflammation reduction. The inflammatory aspect of AD is treated with topical and systemic medications. The effectiveness of each drug depends on the level of AD and how it reacts to other agents. While minimizing negative effects and accommodating patient preferences, one must strive for maximum efficacy [26].

Topical Therapies: Topical corticosteroids (TCSs) have been used for many years and are regarded as the cornerstone of AD treatment. They are used as the initial anti-inflammatory therapy for AD. TCSs are divided into four groups according on their potency. The patient's age, the affected body region, the severity of the condition, and the length of the treatment should all be taken into account when determining the potency and delivery system of the TCSs. TCSs should be used twice daily for the treatment of AD. TCSs are safe and effective for treating AD flare-ups when administered for up to 4 weeks, according to clinical research. But many flare-ups could be effectively managed with a shorter term of therapy (1-2 weeks). In clinical practice, TCS is used with other pharmaceuticals. TCSs and emollients can effectively lower the likelihood of flare-ups when taken as part of maintenance therapy (e.g., intermittent, or twice-weekly dose). Side effects, particularly with highly powerful and potent TCS, can be cutaneous and systemic. Regular physical examinations should be performed on patients using TCS for an extended period of time to check for any cutaneous adverse effects. Strong TCS are not advised for the treatment of AD, especially in young patients [32].

Tacrolimus and pimecrolimus are topical calcineurin inhibitors (TCIs) that are indicated as a second-line anti-inflammatory treatment option for adults and children at least 2 years old who have moderate-to-severe AD (tacrolimus) or mild-to-moderate AD (pimecrolimus) when other topical therapies are insufficient or inappropriate. In certain situations, especially in patients undergoing long-term therapy and on sensitive skin regions, they might be utilized off-label as the first line of treatment. TCSs and TCI can be used together to treat AD. Tacrolimus twice weekly for up to 52 weeks is an effective proactive, intermittent medication for avoiding, postponing, and minimizing flares, which enhances quality of life for AD patients. When using TCIs, a brief burning or stinging sensation is typical; it may be related to the first administration and get better with continuing usage [32].

New topical treatments Delgocitinib ointment is a topical JAK (Janus kinase) inhibitor approved in Japan for the treatment of adult patients with moderate-to-severe AD for up to 28 weeks, and other topical JAK inhibitors (topical tofacitinib and ruxolitinib) appear to be promising treatments for mild-to-moderate AD [33].

Systemic Therapies: Systemic therapy is advised if AD cannot be satisfactorily managed with prescribed topical medications and phototherapy. Patients who often need strong TCS for broad body regions over long periods of time might benefit from it. Systemic corticosteroids, cyclosporine A, azathioprine, mycophenolate mofetil, and methotrexate are among the systemic treatments for AD. Systemic steroids should not be used for an extended period of time. It can, however, be used for brief courses to manage an acute exacerbation. Additionally, the possibility of a flare-up after stopping the systemic steroid should be taken into account [34].

An oral calcineurin inhibitor called CsA is used for moderate-to-severe AD. It may be used off-label in children and adolescent patients with a refractory or severe condition. It is licensed for the treatment of AD in adults in several European countries. The course of therapy might last anything from three months to a year. However, some people might be able to tolerate low-dose CsA for extended periods of time [32].

To treat moderate-to-severe AD, the immunosuppressive drug MTX is often used off-label. After 8–12 weeks of therapy, methotrexate's maximal efficacy is attained. It has a gradual commencement of action. AZA and MMF are two more immunosuppressant that can be used to treat moderate-to-severe AD. In 2017, the US Food and Drug Administration (USFDA) and the Saudi Food and Drug Authority (SFDA) approved dupilumab as the first biologic for patients with moderate-to-severe AD who are not optimally responsive to topical therapies or when those therapies are not recommended, or for patients 6 years of age and older who have treatment failure on one or more oral immunosuppressive drugs [35].

A completely human monoclonal antibody called dupilumab is aimed towards the interleukin (IL)-4 α receptor alpha-subunit. It functions by preventing two important type 2 immune response drivers, IL-4 and IL-13, from signaling. Dupilumab should be taken every day together with emollients, and if necessary, topical anti-inflammatory medications. During the first few weeks after starting dupilumab, standard systemic immunosuppressant may be continued until the complete clinical effect is attained [32].

A suitable and safe treatment option for individuals who are resistant to dupilumab mono-therapy is to combine dupilumab with a conventional medication or phototherapy. The information from the registration trials in clinical practice, addressing effectiveness, safety, and improvement of patient-reported outcomes, has been verified by further real-world research [36].

Baricitinib and upadacitinib (JAK inhibitors) have received approval from the SFDA and the European Medicines Agency (EMA) to treat moderate-to-severe AD in adult patients who are suitable for systemic treatment [37]. On the other hand, the USFDA and SFDA authorized upadacitinib and abrocitinib for use in treating adults and pediatric patients with moderate-to-severe AD who are at least 12 years old. Another completely human monoclonal anti-IL-13 antibody, talokinumab, has just received USFDA and EMA approval for the treatment of moderate-to-severe AD in adults that is not well managed by topical prescription treatments. The SFDA has not yet given its approval [38].

New Therapy in the Plans: For the treatment of AD, monoclonal antibodies such as nemolizumab, lebrikizumab, and fezakinumab that block the actions of different interleukins (IL-4, IL-13, IL-5, IL17, IL-22, IL-31, and IL-33) have shown therapeutic potential [32].

Phototherapy: is an adjunct skin-directed therapy that helps AD patients sleep better. It is seen as a viable therapy option for moderate-to-severe AD, if accessible, when combined with concurrent topical anti-inflammatory treatments. For individuals for whom topical anti-inflammatory medications are inappropriate (i.e., bad response, contraindication), it can also be administered as a mono-therapy. The

best phototherapy treatments for treating AD are narrow-band ultraviolet B (NB-UVB) and ultraviolet A1 (UVA1). Common side effects of phototherapy include actinic damage, local erythema and soreness, pruritus, burning, and stinging [32].

The accessibility, practicability, and lack of effectiveness of phototherapy for lesions on the scalp and folds are its practical constraints. To lessen the frequency of flare-ups, concurrent treatment with topical anti-inflammatory medications, emollients, and phototherapy are suitable choices [32].

4. Conclusion

Receiving initial treatment from AD in the primary care setting is important for managing the AD and offering continuous maintenance care. As a result, it's crucial that physicians understand how to assess, diagnose, and treat AD as well as how to take care of their patients' skin. A comprehensive approach to diagnose the condition, taking into account both the physical aspect of AD and its influence on the patient's quality of life, given the significant burden that AD causes on afflicted patients and their families. As a result, the optimum therapy for AD patients should always take into account an individual management strategy. As a result, brand-new targeted topical and systemic medicines are being created that focus on the root causes of AD and might alter the course of AD treatment.

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