Adjunctive Management of Itch in Atopic Dermatitis

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KEYWORDS

• Atopic dermatitis • Itch • Adjunctive treatment • Topical adjuncts

KEY POINTS

- Itch is the most common and burdensome symptom associated with atopic dermatitis (AD).
- Treatment of AD-associated itch can be challenging, and there is a need for adjunctive management of symptoms to improve quality of life.
- Emerging therapeutic agents may decrease the need for the use of treatments with undesirable side effects, such as topical corticosteroids.

INTRODUCTION

Atopic dermatitis (AD), also known as atopic eczema, is a chronic relapsing inflammatory skin condition that initially takes its toll on children, being seen in 15% to 30% of the pediatric population globally, with a substantial percentage persisting into adulthood.[1,2] The 1-year prevalence of diagnosed AD in adults during the last 2 decades is estimated to be between 1% and 17%.[3] AD flares can present with a wide range of clinical symptoms, most commonly dry skin that is red, itchy, or painful.[4] The most common and burdensome symptom is itching, with 85% to 92% endorsing this daily.[5,6] Itch has a substantial negative impact on quality of life due to its contribution to impaired sleep, reduced social functioning, impaired mental health, and reduced general vitality in AD patients compared to the general population.[7] Due to the complex etiology of AD, treatment can be challenging. There is often a need for adjunctive management of symptoms to reduce burden. The optimal approach must be broad and target multiple points along the itch pathway in addition to addressing external factors.[8] This article will summarize the current literature on the latest therapies used adjunctively to conventional treatment regimens.

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CURRENT GUIDELINES

The foundation of baseline management for most people with AD is the use of emollients or moisturizers to minimize dryness. This method should be done in conjunction with topical corticosteroids (TCS) or topical calcineurin inhibitors such as tacrolimus or pimecrolimus, which work against pruritus by inhibiting T-lymphocyte activation and suppressing the synthesis of pro-inflammatory cytokines.[9] TCS improve itch in patients with AD rapidly, often within 1 to 4 days.[10] However, this is not a viable long-term treatment due to adverse effects.

Crisaborole ointment, a phosphodiesterase inhibitor, and ruxolitinib cream, a Janus kinase (JAK) inhibitor, are also optimized topical therapies for itch in AD.[11]

For those with more severe or widespread disease, oral agents may be required. The first-line systemic agents for AD are biologics.[11] The 2017 Food and Drug Administration (FDA) approval of dupilumab, an injectable monoclonal antibody that inhibits IL-4 and IL-13 signal transduction, has revolutionized the management of AD in individuals 6 months of age and older. The second biologic approved for the treatment of AD is subcutaneous tralokinumab, which targets IL-13 and is approved for patients over the age of 12.[12] According to the most recently updated guidelines for the management of AD, JAK inhibitors are advised for those who fail other systemic therapies.[11] The FDA-approved JAK inhibitors for AD include upadacitinib and abrocitinib, both of which preferentially target JAK-1.[11] A comprehensive treatment algorithm for AD is proposed as depicted in **Fig. 1**.

TOPICAL ADJUNCTS

Damage to the skin barrier facilitates the entry of external pathogens and irritants, triggering inflammation and itch.[13] Utilizing moisturizers may lubricate the skin (emollients), prevent water evaporation (occlusives), and retain water (humectant), counteracting increased transepidermal water loss noted in atopic itchy skin.[14] In addition to the typical ingredients found in moisturizers, several supplemental topical agents work especially well for itch in AD. A summary of topical adjunctive therapies is shown in **Table 1**.

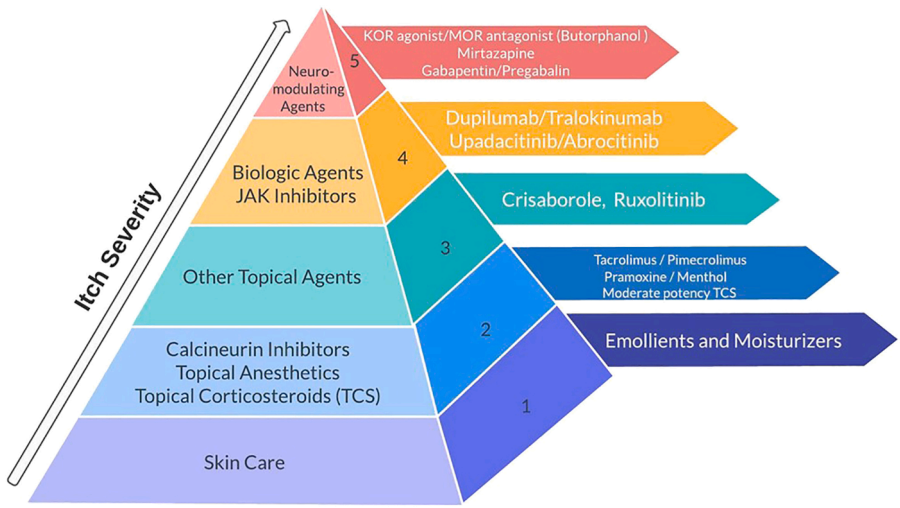

Fig. 1. Management of atopic dermatitis by itch severity.

Table 1
Atopic adjuncts for the management of atopic

Agent	Mechanism	Dose	Notes
Colloidal oatmeal	• Phenols, starches, and β-glucans create and a barrier with anti-itch activity	• 1% Cream or body wash	• Safe and gentle option for young patients
Ceramides	• Replacement of ceramide loss in lipid bilayer of stratum corneum • Restore barrier function	• 0.5%−4%	• May be used in combination with pramoxine and hydrocortisone
Bleach baths	• Restores the skin surface microbiome by eradicating bacteria, especially by decreasing the abundance of *S. aureus*	• Dilute 6% bleach to a concentration of 0.005%	• Does not worsen antibiotic resistance or disrupt epidermal barrier function
Prebiotic/probiotic (synbiotic) baths	• Alters the skin microbiome and decreases skin pH, thus reducing colonization with *S. aureus* that is driven by the increased pH in atopic skin	• Variable	• Lactic acid in particular has shown anti-pruritic effect
Topical anesthetics	• Pramoxine- interferes with impulse transmission along sensory nerve fibers • Lidocaine- inhibits voltage-gated sodium channels, reducing the firing of pruriceptive sensory fibers	• Pramoxine: 1% cream • Lidocaine: 3%–5% cream	• Pramoxine is often combined with ceramide cream for rapid and long-lasting itch relief
Cooling agents	• Menthol- unclear; potential activation of TRPM8 on C-fibers, stimulation of Aδ fibers, or activation of K-opioid receptors • Camphor- TRP activation	• Menthol: 0.5%-3% cream/ointment • Camphor: 0.5%-9% cream/ointment	• Avoid in patients who report worsening of their itch with cold showers • Menthol may irritate the skin when used in higher concentrations • Menthol and camphor are often compounded together

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Table 1
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Agent	Mechanism	Dose	Notes
Mu-opioid receptor (MOR) antagonists	• Blocks the pro-pruritic effect of mu-opioid receptors	• Naltrexone 1% cream	• Further research is needed to evaluate topical vs systemic opiates to treat AD adjunctively • Opiates administered via nasal spray (butorphanol) and orally (difelikefalin) may have greater clinical utility
Cannabinoids	• N-palmitoylethanolamide (PEA)- inhibits endocannabinoid breakdown and reduce mast cell degranulation • Cannabidiol (CBD)- suppresses level of pro-inflammatory cytokines, antimicrobial properties	• 0.3% PEA cream	• CBD products containing <0.3% tetrahydrocannabinol (THC) are legal on the federal level, but it is important to check with state laws before prescribing
Aryl hydrocarbon receptor (AhR) agonists	• Tapinarof- binds directly to the AhR receptor, resulting in suppression of inflammatory cytokines	• 1% Tapinar of cream	• May substitute for coal tar, which can be malodorous and irritating • Promising pruritus reduction from phase III trials (ADORING 1/2) • Long-term safety anticipated by ADORING 3
Phosphodiesterase type 4 (PDE4) inhibitors	• Roflumilast- blocks PDE4 and leads to the accumulation of cyclic adenosine monophosphate (cAMP), resulting in decreased production of proinflammatory mediators/increased production of anti-inflammatory mediators	• 0.15% Roflumilast Cream	• Itch reduction may be seen as early as 24 h following application according to recent phase III trial results (INTEGUMENT 1/2)

Colloidal Oatmeal

The use of 1% colloidal oatmeal cream has been used to treat pruritic dermatoses for centuries and has demonstrated benefit as an adjunctive treatment for itch in AD.[15,16] Oatmeal contains different types of phenols as well as starches and β-D-glucans that help to create an occlusive barrier with anti-itch activity.[17,18] One study found a significant improvement in itching of AD patient at weeks 2, 4, and 8 when oatmeal cream and body wash were added to their normal topical regimen.[19] Colloidal oatmeal cream also appears to be effective in reducing itch when used instead of a patient's usual AD topical regimen.[20]

Ceramides

Ceramides normally make up 50% of the lipid bilayer within the stratum corneum; however, they are significantly reduced in atopic skin.[21] Thus, topical supplementation of ceramides is an implicated therapy for restoring barrier function and relieving certain AD symptoms, specifically itch.[22] Importantly, ceramide reduction is particularly prominent in black skin compared to white and Asian skin.[23] Given that newborns and infants are highly susceptible to skin barrier disruption, and the prevalence of AD in black children has disproportionately increased over the past 2 decades, addressing ceramide imbalance is also an important part of ameliorating racial disparities in childhood eczema.[24,25] One cohort study showed improvement of itch from "very itchy" to itching only when the skin was wet after a twice-daily regimen of ceramide-containing cleanser and moisturizer were used for 6 weeks.[26] Notably, ceramide may be used in combination with other ingredients, such as 1% pramoxine and 1% hydrocortisone, to additively ameliorate itch.[27] There is growing evidence to suggest that ceramides are a safe and effective adjunct for treating AD-associated itch and may be a suitable alternative to avoid or limit steroid-containing substances.[28–30]

Bacteria-Derived Compounds

The skin microbiome is a key player in the regulation of itch via its release of neurochemicals and communication with the skin, brain, and peripheral sensory neurons.[31,32] In AD flares, there is an overall decrease in microbial diversity and a proliferation of certain bacteria, namely *Staphylococcus aureus* (*S aureus*).[33] The non-histaminergic itch pathway in AD can be activated by proteases released following bacteria binding to protease-activated receptors (PAR-2 and PAR-4), which are overexpressed in the itchy skin of AD patients.[34,35] Because of this mechanism, certain therapeutic compounds that limit the overgrowth of bacteria have shown efficacy in reducing inflammation and itch.[36] *Vitreoscilla filiformis*, for example, is a nonpathogenic bacterium found in thermal springs thought to reduce pruritus in patients with AD when applied in a compounded cream by preventing biofilm formation of *S aureus*.[4,37,38] Other bacterial substances that have improved itch in AD patients include derivatives of *Pantoea agglomerans* and *Vitis vinifera* seed extract.[39,40]

Acidification of the Skin

The colonization of *S aureus* at the skin surface in eczema is largely driven by the associated increase in skin pH, often to greater than 6.5, which leads to the activation of PAR-2 receptors and induces itch.[41,42] Therefore, the acidification of skin with low-pH washes and moisturizers, such as lactic acid, can reverse the pH abnormality and reduce itch.[43–46] One recent study evaluated the efficacy of daily symbiotic baths containing 6 viable lactic acid bacteria and prebiotics in 7 patients with AD.[47] On day 9 and day 14, patients reported significantly reduced pruritus compared to placebo.[47]

These results, among others, suggest that lactic acid may be an effective adjuvant topical for pruritus in eczema.[48]

Bleach Baths

Bleach baths (dilute solutions of sodium hypochlorite) have been used for a few decades as an anti-septic therapy for AD.[49,50] More recently, they have further been investigated as an inexpensive adjunctive therapy for patients with AD given their anti-inflammatory and anti-itching effects.[51,52] Infection with *S aureus* is the most frequent complication of AD, and bleach baths are useful in decreasing the abundance of *S aureus* without worsening antibiotic resistance or disrupting epidermal barrier function.[50] A randomized trial investigating the effect of twice-weekly bleach baths in adults with AD demonstrated decreased itch in 80% of subjects after 6 weeks of treatment and 100% of subjects after 12 weeks. Furthermore, 87% of subjects reported improvement in their sleep as subscore of pruritus.[53] Several other studies have reported a varied improvement in AD severity with bleach baths, although additional large clinical trials are needed.[54,55] Current guidelines support the adjunctive use of bleach baths for patients with moderate-to-severe AD, although clinical improvement may only be seen in about one-fifth of patients.[54,56] 10% of patients can be expected to have greater than 50% improvement.[54] Bleach baths are not recommended for mild cases of AD.[56]

PHOTOTHERAPY

Phototherapy for the treatment of pruritus in AD has been well-studied and is concluded to be effective, safe, and tolerable.[57] Narrowband UVB (NB-UVB) has largely replaced broadband UVB in the clinical setting given its low side effect profile and non-inferiority in pruritus reduction.[58,59] Furthermore, NB-UVB appears to reduce pruritus to a greater extent than UVA in patients with chronic AD.[60] Home phototherapy devices are also available and have demonstrated similar efficacy to office-based phototherapy with the added benefit of cost reduction and increased patient adherence.[61] Evidence demonstrating the impact of different types of phototherapy on itch has thus far been largely variable and of low certainty, emphasizing the need for further research in this area.[62]

TOPICAL NEUROMODULATORS

There is a growing body of evidence to suggest that the nervous system plays a substantial role in promoting AD and mediating itch.[63] The use of systemic neuromodulators or topical anesthetics, when used consistently, may be a viable way to dampen itch signaling.[8]

Anesthetics

Topical anesthetics, such as lidocaine, polidocanol, and pramoxine, have shown some efficacy in AD given their anti-inflammatory and anti-pruritic properties.[64] Pramoxine may reduce itch duration and magnitude by interfering with impulse transmission along sensory nerve fibers.

[65,66]Furthermore, pramoxine may be used in combination with other compounds to provide both moisturization and antipruritic effects.[67] Patients with AD who have used daily ceramide cream with 1% pramoxine hydrochloride found it to provide both rapid and long-lasting relief of itch.[27] A striking 87.5% reported relief of nighttime itch.[27] Lidocaine alleviates itch in AD by inhibiting voltage-gated sodium channels, thus reducing the firing of nociceptive and pruriceptive sensory fibers.[8,64] Additionally, a

topical preparation containing 3% polidocanol, an anesthetic surfactant, and 5% urea led to a significant reduction in itch associated with various pruritic skin conditions, including AD, in a multicenter trial.[68] The use of topical anesthetics as an adjunctive treatment in AD requires further large-group studies to assess efficacy.

Cooling Agents

The use of cooling agents as adjunctive treatment may modulate the perception of itch in AD by evoking the sensation of cold. Common cooling agents include menthol, camphor, and phenol.[8] The exact antipruritic mechanism of menthol is not entirely clear, but some postulate the activation of TRPM8 on C-fibers, direct stimulation of A-delta fibers, or activation of kappa-opioid receptors.[69,70] One study assessed the application of 3% menthol-containing cream in 18 patients with AD and reported a significant reduction in itch at 1 month.[71] In another study of 35 children, 7 days of using a sprayable menthol product led to improved itch.[72] Menthol combined with ceramide and polidocanol has also shown efficacy in reducing itch in AD patients within as little as 5 minutes after application.[73] Camphor similarly functions through TRP activation; however, it potentiates both heat and cold sensations and functions at the TRP vanilloid-3 (TRPV3) and TRPM8 ion channels.[74,75] Of note these topicals should not be administered to a subset of patients with atopic eczema, (approximately 30%), who report that cold temperatures or cold showers aggravate their itch.[76] Additional studies are needed to evaluate the efficacy of these agents in AD, especially menthol, as it may act as an irritant to the skin when used in higher concentrations.[77–79]

Cannabinoids

Cannabinoid receptors 1 and 2 (CB1 and CB2) are abundant in cutaneous nerve fibers, mast cells, and keratinocytes.[77] The use of topical compounds containing N-palmitoylethanolamine (PEA), an endocannabinoid-like lipid mediator, has shown relief of pruritus in patients with chronic itch conditions, including AD, likely due in part to the inhibition of endocannabinoid breakdown and the reduction of mast cell degranulation.[78,79] In a large multicentric, prospective, cohort study, patients reported an improved quality of life secondary to reduced pruritus and improved sleep quality with PEA 0.3% cream.[78] Of note, this study also reported that 56% of patients no longer needed to use topical corticosteroids with the addition of PEA, suggesting that this could be a beneficial adjunctive treatment for AD in place of regimens with harsh side effect profiles. One study evaluated topical adelmidrol, an analog of PEA, in a group of 20 pediatric patients with mild AD. Complete lesion clearance was noted in 80% of patients with no side effects, providing some evidence for the safety of these agents in children.[80] However, this was a singular pilot study and additional controlled clinical trials are needed. Phytocannabinoids, such as cannabidiol, are increasingly being studied for their anti-inflammatory effects, and have similarly shown efficacy in reducing the intensity of AD-associated pruritus and other symptoms.[81,82]

Coal Tar and Aryl Hydrocarbon Receptor Agonists

Coal tar has a long history of use in patients with psoriasis and AD for itch reduction, although its use is declining, and its efficacy is only moderate.[83,84] Coal tar activates the aryl hydrocarbon receptors (AhR) in keratinocytes, resulting in the induction of epidermal differentiation, restoration of major skin barrier proteins including filaggrin, and subsequent downregulation of the inflammatory process in the skin.[85] AhR is thus a promising key target for pharmacologic effects.[86]

ANTIHISTAMINES

To date, there is no concrete proof that oral nonsedating antihistamines, such as cetirizine, reduce pruritus in atopic dermatitis, and therefore they are not recommended.[87] The intermittent use of sedating antihistamines such as diphenhydramine and hydroxyzine may be useful for helping patients sleep through the night without waking to scratch.[88] Doxepin is a tricyclic antidepressant that is a potent H1 and H2 antagonist and has been used as adjunctive management in AD. One randomized controlled trial conducted in 270 patients reported relief of pruritus in 85% of patients treated with 5% doxepin cream compared to 57% of the vehicle-treated patients.[89] Nonetheless, its use is limited by sedation from percutaneous absorption and high rates of contact dermatitis.[90] Both topical and oral antihistamines may cause anticholinergic symptoms including dry mouth, blurred vision, and tachycardia.[91] Furthermore, their use may lead to reduced sleep quality and decreased rapid eye movement sleep, which is especially important to consider in children.[88] Given the substantial adverse effects and limited efficacy, antihistamines should be considered lower on the list of adjunctive treatments for AD.

SYSTEMIC NEUROMODULATORS

Serotonin receptors are widely distributed in the skin, including in peripheral sensory nerves, keratinocytes, and mast cells, lending to their reported antipruritic effect in various dermatologic conditions.[92,93] Fluvoxamine and paroxetine are 2 selective serotonin reuptake inhibitors that have demonstrated efficacy in patients with pruritus of varying etiologies.[92] Mirtazapine is a dual-acting antidepressant that blocks both serotonergic and noradrenergic receptors and has additional H1-antihistamine properties.[94] Furthermore, its sedating properties may play a role in nocturnal itch reduction and subsequent improved sleep quality, supporting its use in AD patients with symptom exacerbation during sleep.[95,96]

Antiepileptics such as gabapentin and pregabalin have gained substantial attention in the dermatologic community for treating neuropathic itch. Although AD is not neuropathic in origin, there is significant involvement of neural dysregulation and hypersensitization.[34] Gabapentin and pregabalin act on voltage-gated calcium channels, which subsequently regulate the release of substance P (SP) and calcitonin gene-related peptide (CGRP) and reduce neural sensitization.[97] Studies have found an elevated density of SP-positive dermal nerve fibers and elevated cutaneous levels of SP in patients with itch secondary to AD.[98,99] These findings provide support for the potential role of antiepileptics in treating atopic pruritus.

OPIATES

Mu-opioid receptor (MOR) agonism has a pro-pruritic effect, while kappa-opioid receptor (KOR) agonism has an anti-pruritic effect.[100] Therefore MOR antagonists and KOR agonists may provide therapeutic benefits in reducing pruritus in AD.

Mu-opioid Receptor Modulators

In a series of 2 studies, the efficacy of naltrexone, a MOR antagonist, was tested. In the initial pilot study of 18 patients with varying pruritic conditions including AD, more than 70% of patients experienced significant itch relief after treatment with 1% naltrexone cream.[101] In a subsequent crossover trial of 40 patients with AD, the researchers found that the cream containing naltrexone was 29.4% more effective in reducing pruritus and worked about 30 minutes faster compared to the placebo.[101] Prior studies

have shown comparable results, providing some evidence for the role of peripheral opioid receptors in atopic itch.[102,103] Further research is needed to evaluate whether topical or oral agents would be the most effective adjuncts for treating AD.

Kappa-opioid Receptor Modulators

Dysregulation in the κ-opioid system is thought to contribute to chronic itch by acting on both the peripheral and central nervous systems.[104] We previously reported that butorphanol, a KOR agonist and MOR antagonist, has antipruritic effects in different types of chronic itch including severe AD.[105,106] In a recent phase II clinical trial, 3 oral doses of KOR agonist difelikefalin were evaluated for their impact on pruritus intensity in patients with moderate to severe AD, all of which reduced itch compared to placebo.[107] However, a recent phase III trial did not achieve a significant antipruritic effect. Another KOR agonist of interest includes oral asimadoline, which significantly reduced nighttime itching in a multi-site proof-of-concept RCT of 221 subjects with AD; however, it similarly did not achieve the primary endpoint efficacy in a phase III trial.[108]

COMPLEMENTARY AND ALTERNATIVE THERAPIES

Targeting Stress

In addition to targeting the internal pathways associated with AD, it is important to also address external stressors that may trigger worsening disease. While new drugs may be able to adequately manage symptoms, psychologic stress can lead to a vicious cycle of scratching, provoking the relapse of AD symptoms regardless of any positive drug effect.[109,110] Studies have found that relief of cervical muscle tension and massage therapy may be useful adjunctive therapies.[111,112] In one study assessing the efficacy of massage therapy in young children with AD in addition to their existing topical regimen, 1 month of daily, 20-min sessions led to significant improvement of redness, scaling, lichenification, and pruritus, as well as decreased anxiety levels in both the children and their parents.[112]

Acupuncture

Acupuncture is an alternative therapy involving the insertion of thin needles into the skin.[8] In a recent trial assessing the impact of acupuncture on symptoms of AD, 30 participants underwent 4 weeks of acupuncture and reported significant improvement in itch severity.[113] Despite proof that acupuncture is effective in the management of AD, its mechanism is not entirely known. There is some evidence to show that acupuncture may ameliorate skin inflammation and serotonergic itch through the blockade of serotonin 5-HT2 and 5-HT7 receptors.[114] The antipruritic effects of acupuncture may involve vasodilation or stimulation of inflammatory cell mediators, depletion of neurotransmitters through the activation of C fibers, and reduction of type I hypersensitivity reactions.[115,116]

Dietary Supplements

Omega-3 (n-3) and omega-6 (n-6) are essential fatty acids (FAs) that contribute to the formation of ceramides and thus are important in the maintenance of the optimal skin barrier.[117] The typical western diet tends to favor excess n-6 FAs, potentially resulting in a shortage of n-3 FAs. Given that n-3 FAs are associated with decreased inflammation, this imbalance may lead to the itch associated with AD.[118] Thus, targeting an ideal n-3:n-6 FA ratio through the consumption of healthy food is advised as a feasible, low-risk supplemental regimen.[119] Evening primrose oil and borage oil are other n-6 compounds that are rich in gamma-linolenic acid. When applied topically, these oils can reduce eczema severity and itch.[120,121]

EMERGING TOPICAL THERAPIES

Phosphodiesterase Type 4 Inhibitors

Crisaborole ointment is a phosphodiesterase type 4 (PDE4) inhibitor that is approved for the treatment of mild-to-moderate AD in patients as young as 3 months of age. Given its efficacy and safety as a nonsteroidal topical agent, additional PDE4 inhibitors are under development and entering the market. Roflumilast cream, for instance, is approved for the treatment of plaque psoriasis and recently showed favorable results in a phase III trial for AD. Inhibiting PDE4 has anti-inflammatory as well as an early and distinct antipruritic effect.[122,123] In children aged 2 to 5, roflumilast 0.05% cream provided a quick reduction of itch, with 35.3% of patients achieving a 4-point reduction on the Worst-Itch Numeric Rating Scale at week 4.[124] Recent data from 2 phase III trials (INTEGUMENT-1 and INTEGUMENT-2) demonstrated a rapid and significant reduction in itch in adults and children over the age of 6 with mild to moderate AD following application of roflumilast cream 0.15%.[125] Benefits were seen in as little as 24 hours following the initial application. The cream was well tolerated and had minimal adverse events that were limited to 3.5% of subjects.[125]

Aryl Hydrocarbon Receptor Agonists

Tapinarof is an AhR agonist that has demonstrated significant improvement of pruritus in AD.[126] A phase II trial found that the reduction in pruritus from baseline to each study visit up to week 8 was greater in AD patients treated with tapinarof 1% cream than those treated with vehicle, with a clear separation between the 2 groups emerging at week 2.[127] To date, 2 out of 3 subsequent phase III trials (ADORING 2 and ADORING 1) have reported promising results that are consistent with phase II data. The use of tapinarof 1% cream daily in adults and children as young as 2 years old had a meaningful impact on itch reduction in 52.8% and 55.8% of subjects at week 8, respectively.[128,129] The highly anticipated final trial (ADORING 3) will provide insight into the long-term safety of tapinarof for patients with AD.

SUMMARY AND FUTURE DIRECTIONS

Itch is by far the most common complaint of AD patients. Despite the efficacy of first-line therapies and the ongoing development of new targeted drugs, the itch can still be difficult to control. Furthermore, several widely used therapies such as TCS and immunosuppressants are accompanied by adverse effects that patients would prefer to avoid. Navigating this condition requires therapies to control vicious itch-scratch cycles and minimize the burden on quality of life. The adjunctive management of itch AD is thus an important and comprehensive option that should be offered to all patients when creating a personalized therapeutic approach. The data presented in this review highlight the most up-to-date adjunctive agents with supporting evidence for itch-reduction.

CLINICS CARE POINTS

- Patients with AD should be asked about the severity of their itch and the impact it may be having on their daily activities.
- Patients should be offered adjunctive therapy if itch is not adequately controlled with common agents.
- Clinicians should be prepared to discuss the benefits and risks of adjunctive management when creating a personalized treatment approach.

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