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 ORIGINAL ARTICLE

Attenuation of Atopic Dermatitis in Newborns, Infants, and Children With Prescription Treatment and Ceramide-Containing Skin Care: A Systematic Literature Review and Consensus

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ABSTRACT

Background: Atopic dermatitis (AD) typically starts in infancy and early childhood. The chronic skin disorder is associated with recurrent flares, pruritus, and genetic predisposition. Daily use of moisturizers that contain lipids, such as ceramides, reduces the rate of AD flares and the need for topical steroid treatment. We aimed to provide insights on AD attenuation to tailor AD prescription therapy, skin care, and maintenance treatment to improve pediatric patients with AD and families.

Methods: A panel of 6 pediatric dermatologists and dermatologists who treat neonates, infants, and children developed a consensus paper on AD attenuation for pediatric patients. The modified Delphi process comprised a face-to-face panel meeting and online follow-up to discuss the systematic literature search results and draw from clinical experience and opinion of the panel to adopt and agree on 5 statements.

Results: Understanding the functional properties of newborn and infant skin, discussing skincare product use with parents, and recommending tailored prescription and skincare routines can improve newborn, infant, and children's skin health. Studies on the prophylactic application of moisturizers initiated in early infancy suggest moisturizers may delay rather than prevent AD, especially in high-risk populations and when used continuously. Increasingly there is evidence that moisturizer application reduces the severity of AD and extends the time to flares, which may help attenuate the atopic march. The protective effect of skin care for AD has been observed in studies where its daily use is ongoing; these beneficial effects may be lost in less than 1year after cessation. It is therefore important to emphasize that skin care should be routinely used when counseling patients and caregivers.

Conclusion: Healthcare providers can improve patient outcomes in atopic-prone infants and children by providing instructions regarding the daily benefits of applying skin care with gentle cleansers and moisturizers. Using gentle cleansers and moisturizers containing barrier lipids from birth onward may delay AD occurrence and mitigate severity in predisposed infants.

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INTRODUCTION

Atopic dermatitis (AD) is a common recurrent cutaneous disorder associated with pruritus and genetic predisposition that typically begins in infancy and early childhood.[1] It is unclear if AD is a single disease entity or a spectrum of diseases with a shared phenotype.[1-5] Certain clinical features are highly characteristic of AD, such as morphology, anatomic distribution, marked pruritus, relapsing course and or seasonal variation, associated xerosis, and a personal or family history of atopy.[1-5] Maintaining a healthy skin barrier starting early in life, using daily and ongoing skin care with a gentle cleanser and a lipid-containing moisturizer has been shown to reduce the number of flares and reduce AD severity.[6-8] However, evidence on interventions to prevent AD in pediatric patients is conflicting.

This consensus paper aims to provide insights into the literature about AD attenuation in newborns, infants, and children. We further explore gentle cleansers and moisturizers, particularly ceramide-containing skin care, offering insights into their specific role in attenuating AD as monotherapy or as an adjunct to AD treatment for the pediatric population.

MATERIALS AND METHODS

The consensus project used a modified Delphi process comprising face-to-face (February 10, 2023) discussions followed-up online.[9] The process entailed preparing the project, selecting the panel, and conducting systematic literature searches to inform 15 draft statements.[9] During the meeting, the panel evaluated the draft statements during a workshop. Then, a plenary discussion adopted 5 statements to provide clinical data for pediatric dermatologists, dermatologists, and pediatric healthcare providers.

Systematic Literature Searches

The scope of the literature search comprises the attenuation of AD for newborns, infants, and children and the role of skin care, such as ceramide-containing skin care as a monotherapy or as an adjunct to prescription topical and systemic medication.

The literature review considered clinically relevant materials published in English between January 2010 and December 20, 2022, including randomized controlled trials, other clinical studies, guidelines, consensus papers, and review articles. Systematic literature searches on PubMed and Google Scholar (secondary source) were conducted on December 20-22, 2022, by a researcher/clinician (HA) and a physician/scientist (AA).

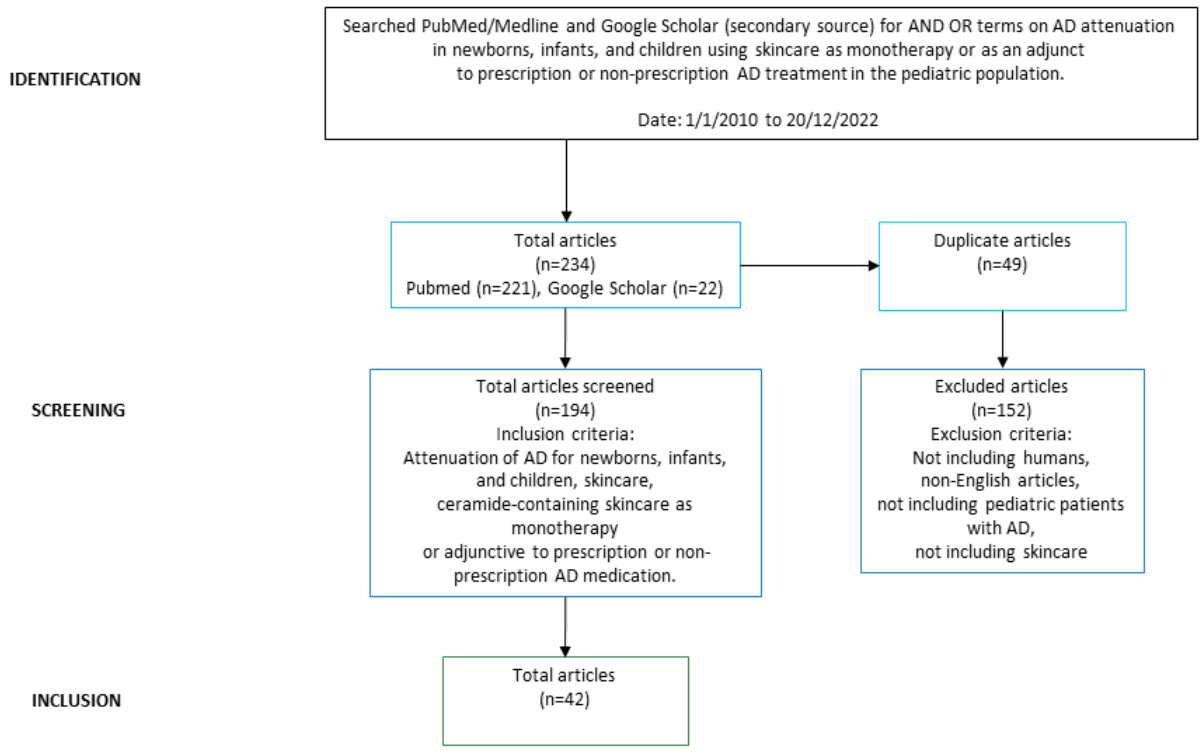
Search terms are provided in Table 1. First, titles and abstracts were reviewed, followed by the full article. The 2 reviewers evaluated results independently, and selected publications were graded based on reviewer consensus. Each selected clinical publication that included skincare information was graded (A, B, or C for study type and 1-4 for likelihood to change confidence in the effect shown).[9]

TABLE 1.

Search Terms: 2 Groups	
Search Terms – Group 1	**Search Terms – Group 2**
Atopic dermatitis AND	Atopic dermatitis AND
neonates OR	neonates OR
infants OR	infants OR
children AND	children AND
atopic march OR	prescription OR
pathogenesis OR	adjunctive OR
guidelines OR	skin care OR
algorithms OR	moisturizer OR
consensus OR	emollient OR
prevention OR	ceramide OR
attenuation OR	skin maturation and moisturization
treatment OR	--
maintenance	--

The 194 studies that met the quality criteria of the literature search informed the creation of 15 draft messaging statements to guide the development of a manuscript. After the panel discussions and online follow-up, a further 152 articles were excluded, leaving n=42 (Figure 1).

FIGURE 1. Systematic literature search results.



RESULTS

Statement 1

Studies have shown that AD-affected skin demonstrated stratum corneum (SC) barrier dysfunction and decreased ceramides and free fatty acid levels. Even the intact skin of a patient with AD that is not flaring is compromised and has impaired barrier function.

AD is characterized by compromised epidermal barrier integrity.[1-5,10]

Research suggests that defects in the skin barrier may be a critical factor in initiating infantile AD and other allergic diseases.[11-13] It has been determined that even the intact, non-flaring skin of a patient with AD is compromised with an impaired barrier function.[1-5] Barrier dysfunction causes a decrease in SC cell adhesion and increased inflammation.[14] The ability of the skin to retain water is decreased, which leads to a cycle of xerosis and itching, scratching, damaged skin, and inflammation.

Filaggrin (FLG) is a filament-binding protein that is essential to the development of the skin barrier and the maintenance of epidermal homeostasis.[15,16] Loss-of-function gene mutations for FLG are a significant risk factor for AD.[16] Clinical studies have identified a relationship between FLG loss-of-function mutations or downregulation, increased transepidermal water loss (TEWL), and infant AD development.[17-19] In a prospective cohort study in 1836 infants, Hoyer et al found an association between FLG loss-of-function mutations (n=166) and the presence of AD at age 3 months (OR 2.89, 95% CI, 1.95-4.28; *P*< .001).[19] Significantly higher TEWL was also observed in the mutation carriers at 6 months (mean 9.68 [95% CI 8.69-10.68]) vs noncarriers (8.24 [95% CI, 7.97-8.15]; *P*<.01).

AD has also been associated with abnormal SC lipid levels, which disrupts lamellar matrices, diminishes skin barrier function, and increases dermal sensitivity to allergens and irritants.[20] Ceramides, in particular, are lipids essential in forming the waterproof barrier of the SC, thereby retaining water in the skin and reducing TEWL.[10] The chain length of very long fatty acids within ceramides is necessary for proper barrier function. Lower levels of longer-chain ceramides and higher levels of shorter-chain ceramides have been found to be expressed in the skin of patients with AD compared to healthy individuals.

Statement 2

As recommended in international guidelines, daily moisturization is an integral part of AD management. Gentle cleansers and moisturizers may improve skin barrier function in AD and reduce skin susceptibility to irritants and xerosis.

Evidence-based international guidelines recommend daily moisturization to treat skin barrier dysfunction and hydrate skin, which is the foundation of AD management.[22-27] According to the US, Canadian, and European guidelines, moisturizers are integral to monotherapy, adjunctive, preventative, and maintenance treatment of AD.[22, 24-27] These guidelines generally support using moisturizers for skin hydration and AD symptom improvement as the primary treatment for mild disease and in conjunction with other agents for moderate-to-severe disease (Table 2).[24]

In treating AD, restoring skin barrier function has long been a therapeutic goal; evidence demonstrating the success of topical moisturizers in these efforts is accumulating. In a double-blind, randomized, vehicle-controlled trial, Boralevi et al investigated the effects of long-term moisturizer therapy on AD-associated xerosis in young children (n=251, age 2-6 years).[6] During a 28-day period, the objective SCORAD score, xerosis score of the SCORAD index, and visual analogue score decreased, and skin hydration increased more in participants in the moisturizer group (n=124) than in the vehicle group (n=125, *P*<.001 for all measures).

Hebert et al conducted a systematic review of clinical trials published between 2006 and 2019 that assessed the treatment of AD with daily moisturization.[23] Studies included in the systematic review evaluated the efficacy of various commercially available moisturizers using endpoints such as TEWL, corneometry, or incidence of flare. These studies showed that moisturizers (typically applied twice daily) significantly improved skin barrier function in children and adults with AD. Studies that conducted side-by-side (split body) comparisons demonstrated that skin barrier integrity was improved with moisturization vs no treatment in nearly all cases (Table 3).

Danby et al performed a randomized, observer-blinded, intra-patient-controlled study investigating a test cream containing triglycerides, ceramides, and cholesterol in a multivesicular emulsion vs a paraffin-based emollient without physiological skin lipids in adults with dry AD-prone skin.[20] Skin areas on the forearm and lower leg treated with the test cream demonstrated a greater increase in skin barrier integrity (effect size for area under the TEWL curve -162, 95% CI, -206 to -118) than that observed with the reference cream. The test cream also reduced TEWL (-15.3 g/m2/h, 95% CI -20.3 to -10.4) and skin sensitivity to sodium lauryl sulfate (-0.5 points visible redness, 97.57% CI, -1.00 to -0.25) compared to the reference cream. Furthermore, lipid chain order was enhanced and associated with skin barrier integrity (r = 0.61) in areas of skin treated with the test cream. The test cream also decreased signs of dryness and increased hydration (8.61 capacitance units, 95% CI, 6.61–10.6) compared to the reference. The investigators concluded that the test cream containing triglycerides, ceramides, and cholesterol facilitated skin barrier restoration and protection from irritation and dryness superior to the paraffin-based reference.

Danby et al also conducted a double-blind, intra-participant, vehicle-controlled study to evaluate the benefits of a test cream and lotion containing ceramides in a multivesicular emulsion for dry skin.[28] Adults with dry, AD-prone skin applied 100 µl of the test lotion or test cream, 3 paraffin-based reference creams (Zerobase, Epimax, or Aquamax), or nothing (control) on 6 treatment sites on the lower leg. Visual dryness and skin hydration scoring were measured at timed intervals (3, 6, 12, and 24 hours after product application). A single application of the ceramide-containing test cream and test lotion increased hydration significantly (P<.001) and reduced skin dryness (P<.05) for 24 hours compared to the control site. The test cream and lotion were the only products tested that sustained clinically meaningful improvements in skin moisturization for 24 hours, reducing the burden of frequently applying moisturizers in managing xerosis in conditions such as AD.

The application of moisturizers is recommended as an integral part of AD prevention, treatment, and maintenance. However, selecting an inappropriate skincare product may be irritating or even worse, cause additional damage to and depletion of dermal intercellular lipids, exacerbating xerosis.[10] Therapeutic moisturizers developed specifically for treating AD symptoms have demonstrated improved skin barrier, reduced susceptibility to irritants, and a decreased incidence of flares in clinical trials.[6-8,11,13,23,29-32] These moisturizers are gentle, non-alkaline, and are specifically formulated to restore the skin barrier, often with physiologic skin lipids, such as ceramides, that maintain and support the skin barrier.[33]

Statement 3

Studies showed that the prophylactic application of moisturizers initiated in early infancy might delay rather than prevent AD

TABLE 2.

Guidelines and Algorithms			
Author/Year	**Type of Patients/ Disease**	**What Was Recommended**	**Key Findings**
Wollenberg A, et al/2018[22]	Adults and children with AD	Frequent, liberal use of emollients should be prescribed as basic therapy for adults and children with AD Emollient soap substitutes and bath oils should be used Emollients with a higher lipid content are preferred during the winter season In mild-to-moderate AD, regular use of emollients has a long- and short-term steroid-sparing effect after AD remission achieved with topical prescription medications	Certain moisturizers improve skin barrier function in AD and protect against irritants Emollients are "the mainstay of management" of AD
Eichenfield LF, et al/2014[24]	Patients with AD	Moisturizers should be used alone, adjunctively, and for prevention and maintenance in AD Moisturizers should be applied soon after bathing and up to TID	Moisturizer monotherapy is appropriate for mild AD Adjunctive use of moisturizers is appropriate for moderate-to-severe AD Moisturizers are important for maintenance treatment and flare prevention in AD
Wollenberg A, et al/2018[25]	Adults and children with AD	Emollients should be prescribed as basic therapy for adults and children with AD	Adjunctive daily use of emollients should be combined with dupilumab treatment
Lansang P, et al/2019[26]	Children with AD	Regular application of emollients should be part of basic daily care Emollients should be applied immediately after daily bathing to maintain skin barrier	AD is a chronic disease that requires ongoing skin care to maintain the skin barrier and prevent flares Early daily application of emollients may reduce or delay the development of AD in high-risk infants
Le Poidevin LM, et al/2019[27]	Patients with AD	Large amounts of moisturizers should be applied BID or TID 2 international guidelines recommend moisturizers with specific ingredients (ie, petrolatum, ceramides, or glycerol)	There was a consensus among 14 international guidelines on the benefits of moisturizer use in AD, even on skin without lesions
Schachner L, et al/2021[33]	Neonates and infants with 3 clinical signs: xerosis, erythema, or erosion/bulla	Monotherapy and adjunctive skin care recommended CER-containing moisturizers are preferred	Non-alkaline cleansers and CER-containing moisturizers used daily maintain a healthy skin barrier and reduce inflammation Gentle moisturizers and cleansers containing barrier lipids help maintain the protective skin barrier when applied from birth onward

Atopic dermatitis (AD), Ceramide-containing moisturizer (CER), 3 times a day (TID), Twice a day (BID)

(moderate certainty), especially in high-risk populations and when used continuously.

Daily use of emollient therapy from birth to enhance skin barrier function may significantly delay the onset of AD in high-risk infants.[11-13,23,26] However, there is some evidence that this treatment may delay rather than prevent AD. Even in the absence of active disease, the chronic nature of AD requires ongoing basic care to maintain the skin barrier.[23,26]

A systematic review and meta-analysis by Zhong et al investigated the efficacy and safety of prophylactic emollients initiated during the first 6 weeks of infancy to prevent AD and food allergies.[34] The review identified randomized controlled trials published between January 2000 and July 2020 that evaluated the effect of prophylactic emollients within the first 6 weeks of life vs no treatment on AD development by 2 years of age. There was no significant reduction in AD development (RR 0.84, 95% CI, 0.64, 1.10) compared to the control group in the 10 studies that fulfilled the inclusion criteria. However, prophylactic moisturizers exhibited an improved skin condition (RR 0.75, 95% CI 0.62-1.11) in infants at high risk for AD development (n = 8 studies). A significant benefit (RR 0.59, 95% CI 0.43, 0.81) was also identified in studies (n = 6) in which emollients were used continuously until AD assessment; however, this effect was not observed if treatment had been interrupted prior to that time. The authors concluded that the application of emollients initiated during the first 6 weeks of infancy — particularly in high-risk populations and with continuous use may delay rather than prevent AD.

Statement 4

Moisturizer use benefits young AD patients, reducing the severity and extending the time to flares. This could help prevent or attenuate the atopic march.

An inhibited barrier function in AD may result in periodic flare-ups of erythematous and pruritic lesions; therefore, delaying or preventing flares is key in managing this disease. AD treatment guidelines recommend daily treatment of atopic skin with moisturizers to prevent flares and maintain a flare-free state.[24,26,27] Van Zuuren et al conducted a systematic review of randomized controlled trials that enrolled people with AD.[29] The review included 77 studies (N=6603; age 4 months to 84 years [mean 18.6 years]; mean treatment duration, 6.7 weeks). When all moisturizers were compared to vehicle, placebo, or no moisturizer, they were found to produce fewer flares (6 studies, n=607; RR 0.33, 95% CI, 0.17 to 0.62; moderate-quality evidence) and lower investigator-assessed disease severity scores (12 studies, n=1281; SMD -1.04, 95% CI,-1.57 to -0.51; high-quality evidence).

In addition, moisturizer combined with active topical treatment was more effective in reducing flares (1 study, n=105; RR 0.43, 95% CI, 0.20 to 0.93; low-quality evidence) and in lowering investigator-assessed disease severity (3 studies, n=192; SMD-0.87, 95% CI, -1.17 to -0.57; moderate-quality evidence) than the active treatment alone. The authors concluded that most moisturizers produce some beneficial effects, prolong time to and decrease the number of flares, and reduce the number of topical steroids needed to diminish eczema severity.

TABLE 3.

Meta-analyses			
Author/Year	**Type of Patients/ Disease**	**What Was Recommended**	**Key Findings**
Van Zuuren EJ, et al/2017[29]	6603 patients with AD, age 4 mo-84 y (mean 18.6 y)	Most moisturizers had some beneficial effects, such as: - prolonging time to AD flares -decreasing number of AD flares - reducing amount of topical steroid needed to reduce AD severity	Compared to vehicle, placebo, or no moisturizer, moisturizers produced: - fewer flares (6 studies, n=607; RR 0.33, 95% CI, 0.17 to 0.62) - lower investigator- assessed disease severity scores (12 studies, n=1281; SMD -1.04, 95% CI, -1.57 to -0.51) - fewer flares when combined with active topical treatment (1 study, n=105; RR 0.43, 95% CI, 0.20 to 0.93) - lower investigator-assessed disease severity scores than active topical treatment alone (3 studies, n=192; SMD -0.87, 95% CI, -1.17 to -0.57)
Zhong Y, et al/2022[34]	3409 infants at high or normal risk for the development of AD	Emollients initiated during first 6 weeks of infancy may prevent AD—particularly in high-risk populations and with continuous use Emollients may delay rather than prevent AD	Emollient use initiated during first 6 wks of infancy did not significantly reduce AD development at 2 yo compared to control (RR 0.84, 95% CI, 0.64, 1.10) Prophylactic moisturizers exhibited a significant benefit (8 studies; RR 0.75, 95% CI 0.62-1.11) in infants at high risk for AD development A significant benefit (6 studies; RR 0.59, 95% CI 0.43, 0.81) was identified when emollients were used continuously until AD assessment at 2 yo; t his effect was not observed if treatment had been interrupted

Atopic dermatitis (AD), Standard mean deviation (SMD), Years of age (yo)

TABLE 4.

Randomized Controlled Trials, Including Skin Care			
Author/Year	**N**	**What Was Studied**	**Key Findings**
Boralevi F, et al/2014[6]	251/children with AD, age 6-12	Effect of moisturizer (n=124) or vehicle (n=125) applied at least QD on AD-associated xerosis	After the 28-day, double-blind period, children receiving moisturizer had a lower objective SCORAD score and decrease in xerosis score than at baseline vs vehicle (66.1% vs 45.6%, respectively; P<.001)
Weber TM, et al/2015[7]	45/infants and children with AD (mean age 3.5 y)	Effect of QD moisturizer and cleanser (n=21) or cleanser only (n=24) applied for 6 mos or until flare	Flare incidence lower in moisturizer + cleanser vs cleanser only group (21% vs 65%; P=.006)
Ma L, et al/2017[8]	64/children with mild-to-moderate AD (age 2-12 y)	Effect of QD CER-containing body wash and BID moisturizer (n=32), or only QD CER-containing body wash (n=32) for 12 wks on flare	Body wash + moisturizer group had nearly 2 mos delay in median time to flare (89 vs. 27 days), earlier onset of action re: fewer flares at wk 4 (31% vs 59%, P = .022), and fewer flares at 12 wks (50% vs 72%, P=.079) vs body wash alone
McClanahan D, et al/2019[11]	100/neonates at high-risk for AD	Development of AD at 12 mo or 2 y after applying QD CER + filaggrin-associated AA-containing emollient (n=54) or emollient of choice (n=46)	AD diagnosed at 12 mos in 13.2% vs 25% (P=.204) and at 2 y in 19.4% vs 31% (P=.296) of participants in each group, respectively; trend in favor of the CER + AA group
Horimukai K, et al/2014[12]	118/neonates at high-risk for AD	Development of AD at 32 wks after QD application of emollient moisturizer (n=59) or petroleum jelly control (n=59)	32% fewer neonates in the emollient group developed AD vs the control group (P = .012, log-rank test)
Simpson EL, et al/2014[13]	124/neonates at high-risk for AD	Development of AD at 6 mos after at least QD application of emollient (n=64) vs no emollient (n=60)	Relative risk reduction of 50% (RR 0.50, 95% CI, 0.28-0.9; P = .017) in the cumulative incidence of AD at 6 mos observed in the emollient group
Chaoimh CN, et al/2022[39]	321/infants at high risk for AD	Effect of BID oat-, fatty acid-, and CER-containing emollient for first 8 wks of life (n=161) vs standard routine skin care (n=160)	Cumulative incidence of AD in the emollient group at 12 mos was 32.8% vs 46.4% in the standard routine skincare group (RR 0.707, 95% CI, 0.516, 0.965; P = .036); early application of an emollient for very dry, AD-prone skin reduced AD incidence in 1 yo high-risk infants
Chalmers JR, et al/2020[41]	1394/neonates at high risk for AD	Effect of at least QD emollient (n=693) or mild cleansers/shampoos (control group, n=701) on incidence of AD at 2 yo	At 2 yo, AD was present in 23% of participants with evaluable data in the emollient group (n=598) and 25% of such infants in the control group (n=612, adjusted RR 0.95, 95% CI, 0.78 to 1.16; P = 0·61; adjusted risk difference -1·2%, -5.9 to 3.6)
Skjerven HO, et al/2020[42]	2397/neonates not selected for atopy	Effect of skin intervention (bath + added oil and face cream applied from age 2 weeks), food intervention (eggs, wheat, cow's milk, + peanut butter introduced between age 12-16 weeks), skin + food intervention, or no intervention (control group) on incidence of AD at age 12mo	At age 12 mos, incidence of AD was 11% in skin intervention group, 9% in food intervention group, 5% in combined intervention group, and 8% in control group (risk differences favored control group); incidence of AD was not reduced by skin or food interventions

Atopic dermatitis (AD), Once a day (QD), Years of age (yo), Months (mo)

A randomized controlled study in Chinese children (N=64, age 2-12 years) with mild-to-moderate AD enrolled participants within 1 week after successful treatment with a topical corticosteroid.[8] Patients were randomly assigned to a group that applied a ceramide-containing body wash and moisturizer once and twice daily, respectively (n=32), or only ceramide-containing body wash once daily (n=32) for 12 weeks. A delay in the median time to AD flare of nearly 2 months was shown for the group applying body wash and moisturizer compared to those using body wash alone (89 vs 27 days, respectively).[8]

A randomized controlled study, investigated the efficacy of 2 non-prescription, steroid-free skincare formulations in relieving the symptoms and reducing the risk of flare in infants and children with AD.[7] Following a 2-week washout period, participants (N=45; mean age 3.5 years [range 3 mos-12 y]) were randomized to apply either the cleanser only (control group) or the cleanser and a daily moisturizing body cream once daily for 6 months or until flaring. The cleanser contains mild surfactants and panthenol and the cream contains colloidal oatmeal, licochalcone A, and ceramide 3. Compared with the control group, the incidence of flaring was significantly lower in the moisturizer plus cleanser group (21% vs 65%; *P*=.006).

The consensus among medical practitioners is that a significant proportion of high-risk children will develop persistent cases of AD and/or other atopic diseases such as allergic rhinitis or asthma. A higher prevalence of rhinitis and asthma[35] or asthma[36] has been associated with more severe AD compared to milder disease. In an Italian cohort of patients with AD (followed 16.9 years on average), the risk of asthma onset increased 4 times in patients with severe AD compared to moderate AD and 2 times in patients with moderate AD compared to mild AD.[36] Data collected in retrospective and prospective cohort studies in patients with severe AD have shown similar results.[37,38] Based on these findings, the ability of moisturizers to help reduce the severity of AD and the incidence of flares in young patients could assist in attenuating atopic march.

Statement 5

When applied from birth onwards, gentle cleansers and moisturizers containing barrier lipids may mitigate AD occurrence and severity in predisposed infants.

A growing body of evidence supports skin care starting early in life, recognizing the benefits of ongoing daily use of non-alkaline cleansers and moisturizers to promote a healthy skin barrier (Table 4). When applied from birth onwards, gentle cleansers and moisturizers containing barrier lipids, like ceramides, help maintain the protective skin barrier and improve xerosis, possibly reducing the severity, delaying the occurrence, or preventing AD development in predisposed infants.[11-13,39,40]

Horimukai et al conducted a randomized, prospective, controlled trial to investigate whether applying a moisturizer during the neonatal period prevents the development of AD.[12] Neonates (n=118) at high risk for AD based on family history were enrolled in this study. During the first 32 weeks of life, an emulsion-type moisturizer (2e) was applied daily to the treatment group (n=59). Study results indicated that 32% fewer neonates receiving the emulsion-type moisturizer had developed AD at week 32 compared to the participants receiving the petroleum jelly control (n=59; *P*=.012, log-rank test). The investigators concluded that daily applying an emollient-type moisturizer decreases the risk of AD in infants during the first 32 weeks of life.

Simpson et al performed a randomized controlled trial in the US and the United Kingdom in neonates (N=124) determined to be at high risk for AD.[13] Starting within 3 weeks of birth, parents in the intervention arm applied full-body emollient therapy (in the UK, sunflower seed oil, Doublebase Gel, or liquid paraffin 50%; in the US, sunflower seed oil, Cetaphil Cream or Aquaphor Healing Ointment) to the neonates (n=64) at least once daily, whereas parents of the neonates in the control arm (n=60) did not apply emollients. This study identified a statistically significant protective effect in the neonates who received daily full-body emollient. In addition, a relative risk reduction of 50% (RR 0.50, 95% CI, 0.28-0.9; *P*=.017) on the cumulative incidence of AD was observed in this group. The investigators concluded that emollient therapy from birth is an effective approach for preventing AD; however, they suggested that this effect needs to be confirmed in larger trials.

Chaoimh et al conducted a randomized controlled clinical trial that investigated the incidence of AD at 12 months in high-risk infants in which emollient was applied daily from birth to 2 months.[39] Infants were identified as high risk for AD based on parental history of AD, asthma, or allergic rhinitis. The newborns were enrolled in the study within 4 days of birth and were randomly assigned to receive either an emollient (containing oat ingredients, ceramides, and fatty acids) specifically formulated for very dry, AD-prone skin twice daily for the first 8 weeks of life (intervention group, n=161), or to standard routine skin care (control group, n=160). In the intervention group, the cumulative incidence of AD at 12 months was 32.8% vs 46.4% in the control group (RR 0.707, 95% CI, 0.516, 0.965; *P*=.036). The investigators concluded that the early application of an emollient specifically formulated for very dry, AD-prone skin until 2 months of age reduces the incidence of AD in high-risk infants at 1 year of age.

McClanahan et al conducted a randomized controlled trial enrolling neonates (n=100) at high risk for AD development based on family history.[11] The intervention group received a once-daily full-body application of a ceramide and FLG-associated amino acid-containing emollient. The control arm used a full-body application of an emollient of their choice for dry skin but was requested not to apply it regularly. In the intervention and the control groups, AD was diagnosed in 13.2% vs 25.0% of the participants at 12 months (*P*=0.204) and 19.4% vs 31.0% at 2 years (*P*=0.296), respectively. Although a favorable trend was observed in the intervention group, it was not statistically significant, possibly because of a lack of power due to under-enrollment. The investigators concluded that the trends observed in this study suggest a protective effect of daily full-body therapy with the study emollient compared to the control.

The results of these studies on the prophylactic application of moisturizers for the prevention of AD in infants demonstrate positive trends, but conclusive evidence is lacking.[12,13,40] A large-scale, randomized controlled study by Chalmers et al in neonates (N=1394) at high risk of developing AD (based on having at least 1 first-degree relative diagnosed with AD, asthma, or allergic rhinitis) failed to confirm these results.[41] Newborns assigned to the intervention group (n=693) received emollient (Doublebase Gel or Diprobase Cream) applied at least once daily, and the control group (n=701) was treated with just mild cleansers or shampoos. The results of this study indicated that at age 2 years, AD was present in 23% of infants with evaluable data in the emollient group (n=598) and 25% of such infants in the control group (n=612; adjusted RR 0.95, 95% CI, 0.78 to 1.16; *P*=0·61; adjusted risk difference -1·2%, -5.9 to 3.6). The authors concluded that the study results provided "no evidence that daily emollient during the first year of life prevents eczema in high-risk children." However, it should be noted that study results were partly based on parent- and patient-reported secondary outcome measures rather than objective ascertainment. These included the parental report of clinical diagnosis/time to onset of AD, parent completion of UK Working Party criteria, and patient-reported severity of eczema.

Skjerven et al conducted a randomized controlled trial that included newborns (N=2397) who were not selected according to atopy.[42] The newborns were randomized at birth into 4 groups: skin intervention (bath with added oil and face cream applied from age 2 weeks), food intervention (eggs, wheat, cow's milk, and peanut butter introduced between age 12-16 weeks), skin + food intervention, or no intervention (control group). By

age 12 months, AD was observed in 11% of the infants in the skin intervention group, 9% in the food intervention group, 5% in the combined intervention group, and 8% in the control group (risk difference of 3.1%, 95% CI, -0.3 to 6.5 for the skin intervention and risk difference of 1.0%, 95% CI, -2.1 to 4.1 for the food intervention, in favor of the control group). The authors concluded that "neither skin emollients nor early complementary feeding reduced development of AD at 12 months."

While the results of the large-scale trials[41,42] may appear nonconfirmatory, it should be noted that using other moisturizer formulations may have produced a different effect.

CONCLUSION

Discussing and recommending optimized skincare products and routines to parents can help attenuate AD in newborn and infant skin. Healthcare providers can improve patient outcomes by providing instruction regarding the benefits of applying clinically tested therapeutic moisturizers daily to improve skin barrier function and help delay, reduce, or maybe prevent AD.[23] The protective effect of skin care for AD has been observed in studies where its daily use is ongoing;[34] these beneficial effects may be lost less than 1 year after cessation.[20] It is therefore important to emphasize that skin care should be routinely used, during and between flares, when counseling patients and caregivers.[26]

DISCLOSURES

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