Pediatrics

Pediatric Atopic Dermatitis: A Review of the Medical Management

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OBJECTIVE: To evaluate the available treatment options for pediatric atopic dermatitis.

DATA SOURCES: A literature review was performed in MEDLINE (1950–February 2010) using the key word atopic dermatitis. The references identified were evaluated in comparative treatment. The references included in this review were limited to studies conducted in children less than 18 years of age and written in the English language.

STUDY SELECTION AND DATA EXTRACTION: All of the literature retrieved that was published within the last 5 years (2005–2010) was included in this review. Other pertinent articles published prior to 2005 were also included.

DATA SYNTHESIS: Atopic dermatitis is a chronic inflammatory skin disorder that usually begins during infancy. Potential causes include irritants such as soap and detergents, food allergens, contact allergens, and skin infections. Emollients, moisturizing agents that inhibit water loss and provide a protective coating, are recommended in all patients with atopic dermatitis. Additionally, emollients may reduce the need to use topical corticosteroids. Patients receiving desonide 0.05% plus an emollient achieved significant reductions in severity scores compared to those receiving desonide 0.05% as monotherapy (80% vs 70%; $p < 0.01$). Topical calcineurin inhibitors are not recommended as first-line therapy in pediatric patients with atopic dermatitis; however, their use in children above 2 years of age who fail to respond to topical corticosteroids may be considered.

CONCLUSIONS: Emollients are recommended in pediatric patients with a diagnosis of atopic dermatitis regardless of symptoms. Topical corticosteroids reduce the inflammation and pruritus associated with atopic dermatitis and are available in several formulations and strengths. Calcineurin inhibitors may be an alternative in children older than 2 years of age who do not respond to topical corticosteroids.

KEY WORDS: atopic dermatitis, eczema, emollients, pediatrics.

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Atopic dermatitis is a chronic inflammatory skin disorder that usually begins during infancy and affects approximately 17% of children.[1] Atopic dermatitis commonly occurs at 2–3 months of age. Fifty percent of pediatric patients will develop atopic dermatitis prior to the age of 1 year; almost all patients are diagnosed by the age of 5 years.[2] *Eczema* and *dermatitis* are used interchangeably to describe this pruritic skin condition. The incidence of atopic dermatitis has been on the rise. The prevalence has tripled since the 1960s, affecting 8.9–20.4% of people born after 1970.[3] Some believe the rising prevalence of atopic dermatitis could be due to the increased use of antibiotics, since normal processes of the innate immune system are impaired.[4]

Research suggests that acquiring infections during early childhood through contact with older siblings may prevent atopic dermatitis.[5] Contact with siblings early in life may lead to the development of antibodies and decrease the hypersensitivity to certain allergens. There is currently no cure for atopic dermatitis; however, both the incidence and prevalence appear to decrease with increasing age.[6]

Treatment with topical corticosteroids and emollients has remained the same in the past 5 decades. Topical corticosteroids provide antiinflammatory properties, whereas emollients are moisturizing agents that inhibit water loss while providing a protective coating. Topical calcineurin inhibitors have provided newer treatment options with fewer adverse effects. Multiple topical therapies have been successful at treating atopic dermatitis; however, understanding the different treatment options will provide clinicians the knowledge necessary to help pediatric patients alleviate the itching, maintain hydration, and prevent secondary infections.

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Etiology

Pediatric patients with atopic dermatitis usually have compromised skin barrier function, defects in their innate immune system, and hypersensitivity to allergens. Compromised skin barrier function may result from a lack of cornified envelope genes, which normally produce covalent bonds between proteins to create a protective barrier. Without cornified envelope genes such as filaggrin, the skin lacks the ability to produce sufficient moisture and adequately remove toxins. The innate immune system may also be altered due to defective T regulatory cells. Defective T regulatory cells cannot adequately control the T1 and T2 helper cell response, ultimately leading to excessive inflammation and atopic dermatitis. Hypersensitivity to certain allergens can result in pruritus. Scratching the affected skin can further irritate the area, which could cause the release of pro-inflammatory cytokines and exacerbate the dermatitis. A genetic component also exists in children with a positive family history for atopic dermatitis, allergic rhinitis, or asthma.[7]

Clinical Manifestations

Major features associated with atopic dermatitis include pruritus that is usually worse in the evening than during the day, an eczematous rash on the face and/or extremities, xerosis, and lichenification. Lichenification is thickened, rough skin that results from repeated rubbing or scratching and is more commonly seen in older children. The papulovesicular rash that presents may become crusted and is described as oozing and erythematous. Between the ages of 2 and 4 years, pediatric patients may undergo remission. However, they may experience relapses or recurring eczematous lesions.[8] Flares, or exacerbations, may occur when pediatric patients are exposed to allergens such as soaps or detergents. Clinical manifestations of flares include increased itching, redness, xerosis, dryness, and overall irritability. Children with moderate-to-severe atopic dermatitis who are being optimally managed with minimal improvement may have certain dietary allergies that trigger flares. Table 1 distinguishes between mild, moderate, and severe atopic dermatitis.[9]

Table 1. Assessing the Severity of Pediatric Atopic Dermatitis[9]

Severity	Symptom
Clear	Normal skin No atopic dermatitis present
Mild	Areas of dry skin Minimal itching, some redness
Moderate	Areas of dry skin Frequent itching, redness present
Severe	Widespread areas of dry skin Persistent itching, redness present

Diagnosis

It is recommended that health-care professionals obtain detailed histories from parents or caregivers regarding the time of onset of atopic dermatitis, previous response to treatment, and impact on quality of life. Other considerations for the diagnosis of atopic dermatitis should include possible contact with inhalants, food allergens, and a positive family history.

Atopic dermatitis may be diagnosed when a child experiences an itchy inflammatory skin condition and at least 3 of the following: (1) onset of eczema at 2 years of age or less, (2) history of allergic rhinitis/asthma/family history of atopic disease in a first-degree relative in children who are less than 4 years of age, (3) history of dry skin within the last 12 months, or (4) visible flexural dermatitis involving the creases of the skin or history of flexural dermatitis.[9] Other factors that may aid in the diagnosis of atopic dermatitis include increased immunoglobulin (Ig) E levels and peripheral eosinophilia. Since IgE mediates type I hypersensitivity reactions, only a minimal amount of IgE is normally present in the serum. Many pediatric patients with atopic diseases, including atopic dermatitis, have elevated serum IgE levels that are 5–20 times greater than normal levels.[10] The majority of pediatric patients with atopic dermatitis also have peripheral blood eosinophilia, which is defined as greater than 300 eosinophils per microliter of blood for pediatric patients.[11,12] Other diseases that may resemble atopic dermatitis include seborrheic dermatitis, contact dermatitis, psoriasis, and scabies.

Complications

Complications of eczema that may occur include secondary bacterial infections, eczema herpeticum, ocular problems such as conjunctivitis and dermatitis of the eyelids, changes in skin pigmentation, scarring, irregular sleep, growth effects, and behavioral changes. Health-care professionals are encouraged to educate parents or caregivers regarding the signs of infection such as weeping, pustules, or fevers. Eczema herpeticum is a serious herpes viral infection that may arise in pediatric patients with atopic dermatitis and is characterized by painful, ulcerated lesions.[13] Sleeplessness occurs in 60% of patients as a result of atopic dermatitis symptoms such as itchiness and soreness. Sleep deprivation may lead to behavioral changes as well as growth disturbances.[14] Ten percent of pediatric patients with severe atopic dermatitis are reported to be below their expected height.[9] Health-care professionals may educate parents or caregivers regarding adequate daily intake of vitamin D and calcium.[8]

Data Sources

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Treatment Options

Treatment of atopic dermatitis is highly individualized and consists of nonpharmacologic management options such as removal of allergens, identification of trigger factors, and a balanced intake of dietary nutrients. Particularly during infancy, appropriate intake of vitamin A may affect the incidence of atopic dermatitis seen in children who have a positive family history of atopy.[15] Furthermore, the use of *Lactobacillus* during pregnancy and while nursing may postpone the onset of atopic dermatitis.[8] Pharmacologic therapy includes the use of emollients, topical corticosteroids, or calcineurin inhibitors. Over-the-counter emollients and topical corticosteroids are available for self-treatment of mild atopic dermatitis. Pharmacists in the community setting may educate parents or caregivers on safely self-treating atopic dermatitis and recommend when it is appropriate to seek treatment by a physician. The goals of self-treatment are to stop the itch-scratch cycle, maintain skin hydration, avoid or minimize factors that trigger or aggravate atopic dermatitis, and prevent secondary infections.[16] If over-the-counter treatment options are not providing adequate relief, the eczematous lesions appear to be infected, or the patient's sleep is frequently disturbed by pruritus, it is appropriate for parents or caregivers to seek treatment by a physician.[9]

EMOLLIENTS

Emollients are moisturizing agents that inhibit water loss and provide a protective coating. Since these agents help restore the integrity of the skin barrier, unscented emollients are recommended for all pediatric patients with atopic dermatitis. Large quantities of emollients can be prescribed (250–500 g/wk) to ensure an adequate amount is available for moisturizing, washing, and bathing.[9] Currently, there are no recommendations regarding the appropriate amount or dosing frequency of emollients, nor are there studies actively comparing the efficacy of emollients versus placebo. Most emollients are available without a prescription in several forms including lotions, creams, and ointments. The active ingredients commonly seen in emollients are mineral oil, petrolatum, ceramide, and urea. Ceramide is a lipid found in the stratum corneum of the skin that replenishes lipids, cholesterol, and free fatty acids, thereby alleviating xerosis. One study suggests that ceramide may improve pruritus and the sleep habits of pediatric patients with atopic dermatitis.[17] Urea is a keratolic topical agent improving skin moisture by dissolving keratin. Table 2[16] lists a variety of emollients that can be purchased over-the-counter or with a prescription.

N-Palmitoylethanolamide (Mimyx) is a prescription emollient used to relieve the burning and itching associated with atopic dermatitis. Its ingredients include glycerin; olive oil; palmitamide monoethanolamine (MEA), a conditioning agent; and hydrogenated lecithin, an emulsifier. Olive oil contains fatty acids that coat and protect skin, while glycerin increases moisture, thereby restoring the defective skin barrier and alleviating dry, waxy skin.[18] A potential benefit of *N*-palmitoylethanolamide compared to conventional over-the counter emollients is that it lacks excipients that may irritate skin.[19] An observational, prospective cohort study was conducted to evaluate the efficacy and safety of *N*-palmitoylethanolamide in 923 pediatric patients (≤12 y). The study drug was applied to the affected area(s) at least twice daily as needed for 4–6 weeks to retain moisture. Physicians evaluated the severity of atopic dermatitis using a 4-point scale (0 = no eczema present) taking into account lichenification, itching, dryness, and erythema. Patients also evaluated their atopic dermatitis using questionnaires. A total of 545 patients reported ongoing topical corticosteroid use at baseline. Approximately 34% (183/545) of patients who had been using topical corticosteroids regularly discontinued their steroid use. There was a statistically significant difference in the physicians' scores of atopic dermatitis severity at study end compared to baseline ($p < 0.001$). More specifically, 60.5% of the children experienced improvements in their atopic dermatitis severity scores upon study completion. According to patients' self-evaluations, pruritus improved after 6 days of treatment (45.6%) and at study end (60%) ($p < 0.001$).[19]

Skin Barrier (EpiCeram) is another prescription emollient used to relieve the itchiness and dryness associated with atopic dermatitis. An important active ingredient found in Skin Barrier is hydroxypropyl bispalmitamide MEA, which is also referred to as ceramide. Other ingredients found in Skin Barrier include glycerin and petrolatum.[20] The product also normalizes the pH of the skin and improves the healing response by allowing vapor permeability. Skin Barrier can be applied to the affected area(s) 2 times per day. Adverse effects include tingling upon application. A clinical trial conducted in 121 pediatric patients aged 6 months–18 years evaluated the efficacy of Skin Barrier (n = 59) versus fluticasone propionate 0.05% (n = 62).[17] The SCORing Atopic Dermatitis (SCORAD) index was used to assess the severity of atopic dermatitis. A score of less than 15 was considered mild eczema and a score of

greater than 40 was considered severe eczema. SCORAD scores, sleep scores, and pruritus scores were recorded at baseline and on days 14 and 28. On day 28, both agents showed a statistically significant ($p < 0.0001$) improvement in SCORAD scores. Patients receiving Skin Barrier had a 50.7% reduction in SCORAD scores, while those receiving fluticasone propionate had a 66.7% reduction in SCORAD scores when comparing day 28 to baseline (ANOVA $p = 0.134$, rank sum $p = 0.363$). However, fluticasone (57.6%) showed a statistically significant improvement in SCORAD scores at day 14 when compared to Skin Barrier (36.%) ($p < 0.05$). There were no statistically significant differences between the 2 agents in pruritus or sleep scores at days 14 and 28.

TOPICAL CORTICOSTEROIDS

Topical corticosteroids are antiinflammatory agents that can be applied to actively affected areas once or twice daily. Table 3 lists the topical corticosteroids available according to strength and potency.[21,22] Different strengths are recommended based on the severity of the dermatitis. As described earlier, Table 1 summarizes the definitions of clear, mild, moderate, and severe atopic dermatitis to help clinicians select the appropriate topical corticosteroids. Adverse reactions are rare if corticosteroids are used properly and include stinging upon application, skin atrophy, acne, folliculitis, bacterial infection, and hypertrichosis. Some studies suggest that high-potency steroids may suppress the adrenal axis; however, these studies were not adequately powered to determine the duration of use associated with an increased risk for adrenal suppression.[9] Adverse effects are more likely to occur with increased duration of use, selection of more potent topical corticosteroids, use in areas with thinner skin, and application over larger body surface areas.

Treatment may differ depending on the location of the dermatitis. Table 4 summarizes the appropriate treatment of atopic dermatitis according to location.[9] Low-potency preparations are used for the face and neck; however, medium-potency preparations may be used on these areas for a short period of time (3–5 days) if the patient is experiencing a severe flare. If the eczema is located in the axilla or groin region, medium- or high-potency topical corticosteroids may be used for 7–14 days. Long-term use of high-potency products should be avoided in the axilla or groin region. If improvement is not seen within 7–14 days, secondary infections can

Table 2. Emollients[16]

Brand Name	Primary Ingredients
Absorbase Ointment[a]	Petrolatum, mineral oil, ceresin wax, wool wax alcohol, potassium sorbate
Aquaphor Ointment	Petrolatum 41%, water
Aveeno Moisturizing Bath Treatment Formula[a]	Mineral oil, colloidal oatmeal 43%
Aveeno Moisturizing Cream/Lotion[a]	Petrolatum, dimethicone, isopropyl palmitate, cetyl alcohol, colloidal oatmeal 1%, glycerin
Aveeno Advanced Care Moisturizing Cream	Glycerin, panthenol, petrolatum, isopropyl palmitate, cetearyl alcohol, dimethicone, avena sativa (oat) kernel flour (oat), avena sativa (oat) kernel oil (oat), ceramide 3, avena sativa (oat) kernel extract (oat)
Carmol 10 Lotion	Urea 10%
Carmol 20 Cream	Urea 20%
Cetaphil Gentle Cleansing Bar[a]	Sodium cocoyl isethionate, stearic acid, sodium tallousate, PEG-20, petrolatum
Epiceram[20,b]	Capric acid, cholesterol, glycerin, ceramide, petrolatum
Eucerin Cream[a]	Petrolatum, mineral oil, mineral wax, wool wax alcohol
Jergens Advanced Therapy Ultra Healing Lotion	Petrolatum, mineral oil, dimethicone, cetearyl alcohol, cetyl alcohol, glycerin, allantoin
Keri Original Formula Therapeutic Dry Skin Lotion	Mineral oil, lanolin oil, glyceryl stearate, propylene glycol
Lac-Hydrin Five Lotion	Urea 5%
Lubriderm Advanced Therapy Lotion	Cetyl alcohol, glycerin, mineral oil, PEG-40, emulsifying wax, vitamin E
Lubriderm Bath and Shower Oil	Mineral oil
Lubriderm Daily Moisturizing Lotion	Mineral oil, petrolatum, sorbitol, lanolin, lanolin alcohol, triethanolamine
Mimyx[18,b]	*N*-palmitoyl ethanolamine, olive oil, sarcosine, squalene, pentylene glycol
Moisturel Cream/Lotion[a]	Petrolatum, dimethicone, cetyl alcohol, glycerine
Nivea Body Lotion	Mineral oil, glycerin isopropyl palmitate, vitamin E, lanolin alcohol
Sarna Anti-Itch Lotion	Camphor 0.5%, menthol 0.5%, carbomer 940, cetyl alcohol, dimethylol dimethyl hydantoin, glyceryl stearate, petrolatum
Vaseline Dermatology Formula Lotion	White petrolatum 5%, mineral oil 4%, dimethicone 1%, glyceryl stearate, cetyl alcohol, glycerin

PEG = polyethylene glycol.
[a]Fragrance-free emollients.
[b]Prescription-only emollients.

Table 3. Some Topical Drugs for Atopic Dermatitis[21,22]

Drug	Vehicle
Calcineurin inhibitors	
Pimecrolimus 1% (Elidel; Novartis)	Cream
Tacrolimus 0.03% (Protopic; Astellas)	Ointment
Tacrolimus 0.1% (Protopic; Astellas)	Ointment
Corticosteroids	
Super-high potency	
Betamethasone dipropionate augmented 0.05%	
generic	Ointment, lotion, gel
Diprolene (Schering-Plough)	Ointment, gel
Clobetasol propionate 0.05%	
generic	Cream, ointment, gel, foam, solution
Cormax (Watson)	Ointment, solution
Clobex (Galderma)	Lotion, spray, shampoo
Olux (Connetics Corp.)	Foam
Temovate (GSK)	Cream, solution, ointment, gel
Fluocinonide 0.1% (Vanos; Medicis)	Cream
Halobetasol propionate 0.05%	
generic	Cream, ointment
Ultravate (Ranbaxy)	Cream, ointment
High potency	
Amcinonide 0.1% (generic)	Ointment
Betamethasone dipropionate 0.05%	
augmented generic	Cream
Diprolene AF (Schering-Plough)	Cream
Betamethasone dipropionate 0.05% (generic)	Ointment
Desoximetasone 0.25%	
generic	Cream, gel, ointment
Topicort (Taro)	Cream, gel, ointment
Desoximetasone 0.05%	
generic	Gel
Topicort 0.05% (Taro)	Gel
Diflorasone diacetate 0.05% (generic)	Ointment
Fluocinonide 0.05% (generic)	Gel, ointment, solution, cream
Halcinonide 0.1% (Halog; Ranbaxy)	Cream, ointment
Mometasone furoate 0.1%	
generic	Ointment
Elocon (Schering-Plough)	Ointment
Triamcinolone acetonide 0.5% (generic)	Ointment
Medium-high potency	
Amcinonide 0.1% (generic)	Cream, lotion
Betamethasone dipropionate 0.05% (generic)	Cream
Betamethasone valerate 0.1% (generic)	Ointment
Desoximetasone 0.05% (generic)	Cream
Diflorasone diacetate 0.05% (generic)	Cream
Fluocinonide emollient 0.05% (generic)	Cream
Fluticasone propionate 0.005%	
generic	Ointment
Cutivate (PharmDerm)	
Triamcinolone acetonide 0.1% (generic)	Ointment
Triamcinolone acetonide 0.5% (generic)	Cream

(continued on next column)

Table 3. Some Topical Drugs for Atopic Dermatitis[21,22] (continued)

Drug	Vehicle
Medium potency	
Betamethasone valerate 0.12% (Luxiq; Stiefel Labs)	Foam
Fluocinolone acetonide 0.025% (generic)	Ointment
Hydrocortisone valerate 0.2%	
generic	Ointment
Westcort (Ranbaxy)	Ointment
Mometasone furoate 0.1%	
generic	Cream, lotion
Elocon (Schering-Plough)	Cream, lotion
Triamcinolone acetonide 0.1% (generic)	Cream
Medium-low potency	
Betamethasone dipropionate 0.05% (generic)	Lotion
Betamethasone valerate 0.1% (generic)	Cream
Desonide 0.05%	
generic	Ointment
Desowen (Galderma)	
Fluocinolone acetonide 0.025% (generic)	Cream
Flurandrenolide 0.05%	
Cordran (Aqua)	Lotion
Cordran SP (Aqua)	Cream
Fluticasone propionate 0.05% (generic)	Cream
Hydrocortisone butyrate 0.1%	
generic	Cream, ointment, solution
Locoid (Triax)	Cream
Locoid Lipocream (Triax)	Cream
Hydrocortisone valerate 0.2% (generic)	Cream
Prednicarbate 0.1%	
generic	Cream
Dermatop (Dermik)	
Triamcinolone acetonide 0.025% (generic)	Ointment
Triamcinolone acetonide 0.1% (generic)	Lotion
Low potency	
Alclometasone dipropionate 0.05%	
generic	Cream, ointment
Aclovate (GSK)	Cream, ointment
Betamethasone valerate 0.1% (generic)	Lotion
Clocortolone 0.1% (Cloderm; Valeant)	Cream
Desonide 0.05%	
generic	Cream, lotion
Desonate (Intendis)	Gel
DesOwen (Galderma)	Cream, lotion
Verdeso (Stiefel Labs)	Foam
Fluocinolone acetonide 0.01% (generic)	Cream, solution
Triamcinolone acetonide 0.025% (generic)	Cream, lotion
Lowest potency[a]	
Hydrocortisone 0.5% (generic)[b]	Cream, ointment, lotion
Hydrocortisone 1.0% (generic)[b]	Cream, ointment, lotion
Hydrocortisone 2.5% (generic)	Cream, ointment, lotion

[a]May be ineffective for some indications.
[b]Available without a prescription.

be considered and may occur due to the presence of *Staphylococcus aureus*. Super-high potency preparations are recommended in children only upon the advice of a dermatologist. Some children may experience frequent exacerbations or flares occurring up to 2–3 times per month. When active dermatitis is not present in children with frequent exacerbations, health-care professionals may recommend the intermittent application of topical corticosteroids to commonly affected areas 1 or 2 days each week.[8,9] According to the National Collaborating Centre for Women's and Children's Health guidelines, this strategy may be reassessed for its effectiveness after 3–6 months of prophylactic use.[9]

Comparison of Topical Corticosteroids and Emollients

One study compared desonide 0.05% plus an emollient with desonide 0.05% alone for the treatment of pediatric atopic dermatitis.[23] Efficacy outcomes were measured using a scoring system that rated the severity of atopic dermatitis signs and symptoms. Symptoms were ranked using a scale from 0 to 9; a score of 9 indicated severe symptoms. The total score was developed by taking the sum of 7 variables: erythema, dryness, lichenification, pruritus, excoriations, papules, and crusting. Pediatric patients using desonide 0.05% plus an emollient versus desonide 0.05% alone had a significant reduction in severity scores (80% vs 70%; $p < 0.01$). Adverse effects such as burning or stinging were similar between treatment groups.

Another trial enrolled 173 infants who received topical corticosteroids alone or in combination with emollients for 6 weeks. Patients were evaluated using the SCORAD method. Infants who received emollients had a 46% reduction in the use of high-potency corticosteroids ($p < 0.05$). There was no statistically significant difference in the use of medium-potency corticosteroids.[24]

Randomized Clinical Trials Comparing Different Topical Corticosteroids

Several randomized trials exist comparing the effectiveness of different topical corticosteroid potencies in pediatric patients. A double-blind randomized clinical trial was conducted in 43 children to compare the efficacy of alclometasone dipropionate 0.05% versus clobetasone butyrate 0.05%.[25] No statistically significant difference was found in terms of efficacy. Signs and symptoms of atopic dermatitis were similar in both groups. Another study compared the efficacy of fluticasone propionate 0.05% with hydrocortisone 17-butyrate 0.1%.[26] Pediatric patients experiencing flares applied corticosteroids twice a day for 2–4 weeks and continued use intermittently for up to 12 weeks. Assessment was determined by the total atopic dermatitis score, which took into account the surface area that was eczematous and the severity of the dermatitis. Erythema, excoriation, and lichenification were also accounted for with a maximum possible score of 21. The difference between total scores favored fluticasone propionate 0.05% over hydrocortisone 17-butyrate 0.1% (–1.25; 95% CI –2.46 to –0.05; $p = 0.042$). Itchiness and sleep disturbances were better improved in patients treated with fluticasone propionate. However, no statistically significant difference in the relief of rash between the 2 groups ($p = 0.056$) was observed. Some children in the fluticasone group experienced folliculitis, tinea, and red papules, while minor skin infections such as impetigo were seen in the hydrocortisone 17-butyrate group.

Table 5 lists the clinical trials comparing topical corticosteroids in pediatric patients.[27-30] Some high-potency agents such as triamcinolone acetonide 0.1% were more efficacious than low-potency agents such as alclometasone dipropionate 0.5%. Other high-potency agents showed no

Table 4. Treatment of Pediatric Atopic Dermatitis[9]

Classification	Location of Atopic Dermatitis	
	Face and Neck	Body
Clear	Emollients	Emollients
Mild	Emollients and/or mild-potency topical corticosteroids	Emollients Mild-potency topical corticosteroids
Moderate	Emollients Mild-potency topical corticosteroids Moderate-potency topical corticosteroids are recommended during severe exacerbations for a maximum of 3–5 days Topical calcineurin inhibitors Bandages	Emollients Moderate-potency topical corticosteroids are recommended for only 7–14 days if atopic dermatitis is located on axillae or groin Tacrolimus Bandages
Severe	Emollients Topical calcineurin inhibitors Bandages Phototherapy Systemic therapy	Emollients Potent topical corticosteroids are recommended for only 7–14 days if atopic dermatitis is located on axillae or groin Tacrolimus Bandages Phototherapy Systemic therapy

statistically significant difference in efficacy outcomes when compared to medium-potency agents. For example, fluticasone propionate 0.05% cream versus clobetasone butyrate 0.05% cream did not show any significant differences in outcomes.

TOPICAL CALCINEURIN INHIBITORS

By inhibiting calcineurin, tacrolimus and pimecrolimus prevent the activation of T cells and production of cytokines, thereby reducing the inflammatory effects commonly seen with atopic dermatitis. Topical tacrolimus is available in concentrations of 0.1% and 0.03%. Tacrolimus 0.03% ointment is primarily recommended in children since adverse effects occur more frequently in pediatric patients using tacrolimus 0.1% than in those using 0.03% over long periods of time.[31,32] Topical pimecrolimus is available as a 1% cream.

In a randomized clinical trial, 141 pediatric patients aged 2–17 years applied topical pimecrolimus 1% (n = 71) or topical tacrolimus 0.03% (n = 70) twice daily for 6 weeks.[33] Efficacy outcomes were measured using an investigator's global assessment score and patient questionnaires. The Investigator's Global Assessment is a scoring index from 0 to 5 that rates the severity of atopic dermatitis. A score of 0 represents complete clearance of disease and a score of 3 represents moderate atopic dermatitis. After 43 days of treatment, 30 patients applying topical pimecrolimus and 42 patients applying topical tacrolimus had clear or almost clear dermatitis (p = 0.119). Statistically significant differences in irritation between the 2 agents favored pimecrolimus. More patients receiving tacrolimus (18.5%) experienced irritation compared to those receiving pimecrolimus (8.5%) (p = 0.039). Topical tacrolimus and pimecrolimus are not recommended as first-line therapy in atopic dermatitis. There were reports of malignancies associated with these agents, such as lymphomas, but no causal link was established.[34] As a result, these agents may be recommended in children who do not respond to topical corticosteroids and who are at least 2 years of age. They may be considered if a pediatric patient has had an adverse reaction to topical corticosteroids, such as irreversible skin atrophy. Children with facial eczema who are using corticosteroids for long periods of time may consider tacrolimus or pimecrolimus. Studies have compared topical corticosteroids with tacrolimus (Table 6).[35] A Phase 3, randomized, double-blind, multicenter clinical trial comparing tacrolimus 0.03% and 0.1% ointment with hydrocortisone acetate 1% ointment was performed in 560 pediatric patients (2–15 y) with moderate-to-severe atopic dermatitis.[36] Treatment consisted of ointment applied twice daily for 3 weeks. Pediatric patients were evaluated on days 0, 3, and 7 and on weeks 2, 3, and 2 weeks after treatment ended. The modified eczema area and severity index (mEASI) was used to evaluate the efficacy of the agents used and required investigators to evaluate each patient's head and neck, trunk, upper limbs, and lower limbs for atopic dermatitis. The mEASI score (100% at baseline) is calculated by taking the following factors into account: (1) a score (0–3) assigned based on investigators' evaluation of patients' erythema, edema/indurations, excoriations, and lichenification, (2) a score (0–6) assigned based on the percentage of the total body surface area affected by atopic dermatitis (0–100%), and (3) a score (0–3) assigned based on pediatric patients' assessment of pruritus. Baseline characteristics were well matched among the 3 groups, with the

Table 5. Comparison of Topical Corticosteroids for the Treatment of Pediatric Atopic Dermatitis

Randomized Clinical Trial	Study Design	Results
Triamcinolone acetonide 0.1% cream vs alclometasone dipropionate 0.5% cream[27]	Comparison of the efficacy of these agents and their systemic effects (N = 40); triamcinolone acetonide 0.1% applied twice daily; alclometasone dipropionate 0.5% applied twice daily; treatment up to 3 wk	Greater improvements seen with triamcinolone acetate 0.1% when assessing dermatitis severity scores; no significant differences found in cortisol levels; no adverse drug reactions reported
Mometasone furoate 0.1% vs clobetasone 0.05%[28]	Comparison to determine which corticosteroid has better antiinflammatory properties (N = 60); mometasone applied once daily; clobetasone applied twice daily; 3 wk of treatment	Greater improvements seen with mometasone 0.1% (86% vs 66%; p < 0.01); no adverse effects reported
Fluticasone propionate 0.05% cream vs clobetasone butyrate 0.05% cream[29]	Comparison of the efficacy and safety of these agents (N = 22); fluticasone applied once daily; clobetasone butyrate applied twice daily; 4 wk of treatment	No significant differences in outcomes between pediatric patients receiving fluticasone 0.05% and those receiving clobetasone 0.05%; no significant HPA axis suppression with fluticasone; topical adverse drug reactions not reported
Hydrocortisone butyrate 0.1% vs alclometasone dipropionate 0.05%[30]	Evaluation of the efficacy of both agents (N = 40)	No significant difference in signs and symptoms between pediatric patients receiving hydrocortisone butyrate 0.1% and those receiving alclometasone dipropionate 0.05%

HPA = hypothalamic–pituitary–adrenal.

exception of the median duration of the current episode of atopic dermatitis: hydrocortisone 1% arm, 10.9 months; tacrolimus 0.03%, 6.4 months; and tacrolimus 0.1%, 6.2 months. Pediatric patients randomized to receive tacrolimus 0.03% (n = 189) had a median mEASI score of 55.2%, while those receiving tacrolimus 0.1% (n = 186) had a median mEASI score of 60.2%. Patients randomized to receive hydrocortisone 1% had a median mEASI score of 36.0%. Tacrolimus 0.03% and 0.1% were more effective than hydrocortisone 1% ($p < 0.001$). Skin burning was an adverse effect that occurred more frequently with tacrolimus 0.03% (18.5%) and 0.1% (20.4%) than with hydrocortisone 1% (13%) ($p < 0.05$).There are limited data comparing high-potency topical corticosteroids with tacrolimus and there are no reported studies comparing topical corticosteroids with pimecrolimus.

SYSTEMIC TREATMENTS

Systemic corticosteroids are recommended in severe cases of atopic dermatitis when other treatments have failed. Oral prednisone improves atopic dermatitis, but rebound flares often occur, making the use of systemic steroid treatment less practical.[37] Tapering of systemic corticosteroids is necessary to prevent the occurrence of rebound eczema. A 7-year-old girl with severe eczema was successfully treated with prednisone 5 mg every other day after failing treatment with high-potency topical corticosteroids and emollients.[38] If systemic corticosteroids are administered for less than 1 week, tapering is not necessary. Children receiving systemic corticosteroids for less than 1 month require tapering over 7–14 days until the physiologic dose (10 mg/m²/24 h) is achieved, followed by continued tapering until discontinuation. Children receiving systemic corticosteroids for greater than 1 month require tapering every 15–30 days until the physiologic dose is achieved, followed by continued tapering until discontinuation.[39] Adverse effects associated with systemic treatment include hypothalamic–pituitary–adrenal axis suppression, growth suppression, glucose intolerance, and hypertension. Currently, there is no evidence comparing the use of systemic corticosteroids with topical calcineurin inhibitors or evaluating combination therapy with systemic corticosteroids and topical calcineurin inhibitors.

ORAL ANTIHISTAMINES

The use of oral antihistamines may be beneficial for children who have concurrent allergic rhinoconjunctivitis or dermatographism. Evidence supporting the efficacy of oral antihistamines in children with atopic dermatitis is lacking. These agents may not relieve itchiness or urticarial symptoms caused by atopic dermatitis, although sedating antihistamines may improve pediatric patients' quality of sleep.[8]

BANDAGES

Although dry bandages are widely used, there are no reported clinical trials assessing their benefit in pediatric patients with atopic dermatitis. Advantages of using dry bandages are their ability to allow emollients to remain on the application site, and they can be helpful for children with lichenification of the skin. Dry bandages may be used with emollients and topical corticosteroids but are recommended for only short periods of time (7–10 days). Disadvantages include cost and their application may be time consuming. Dry bandages are not recommended for treatment of an infected eczematous lesion. Wet wrap treatment can be used in pediatric patients who have severe atopic dermatitis, extremely dry skin, or exacerbations that are not well controlled by topical agents, or for children who tend to scratch limbs extensively at night. Wet wrap treatment consists of 2 layers of open-weave tubular bandages. One layer is soaked in warm water and placed on top of the affected area(s) after topical agents are applied. The second, dry layer is placed on top of the wet bandage. Clinical trials did not show any evidence that wet wrap therapy is better than conventional treatment with topical corticosteroids and emollients.[40] Table 7 summarizes results of clinical trials that compared topical corticosteroids plus emollients to topical steroids plus wet wrap therapy.

PHOTOTHERAPY

Phototherapy is an option for pediatric patients with severe atopic dermatitis who are nonresponsive to other therapy, but there are minimal data regarding its effectiveness. In addition, relapse commonly occurs once phototherapy is discontinued.[8] Phototherapy consists of exposure to ultraviolet light and is theorized to have some immunosuppres-

Table 6. Comparison of Topical Corticosteroid and Topical Calcineurin Inhibitor for the Treatment of Pediatric Atopic Dermatitis[35]

Randomized Clinical Trial	Study Design	Results
Tacrolimus 0.03% vs hydrocortisone acetate 1%	Comparison of the safety and efficacy of these agents in pediatric patients with moderate-to-severe eczema (N = 624); tacrolimus applied once or twice daily; hydrocortisone applied twice daily; 3 wk of treatment	Tacrolimus was significantly more effective than hydrocortisone 1% in severity scores; adverse effect of skin burning was significantly higher in tacrolimus group

sive effects. Guidelines for the management of atopic eczema in children developed by the National Institute for Health and Clinical Excellence indicate that the use of phototherapy is appropriate when other treatment options have failed.[9] Phototherapy is contraindicated in pediatric patients with a family history of skin cancer and in those more susceptible to adverse effects such as burning or blistering (ie, very fair skin). Risks associated with one course of phototherapy are very low.[41]

BLEACH BATHS

S. aureus is colonized in the majority of pediatric patients with atopic dermatitis and may be a result of a compromised skin barrier, defects in the innate immune system, reduced skin lipid content, and the pH of the skin surface.[42] Pediatric patients may experience exacerbations of atopic dermatitis as a result of *S. aureus* overgrowth.[43,44] Oral antibiotics may reduce colonization with *S. aureus*, but evidence demonstrating clinical improvement of atopic dermatitis is minimal.[8] Health-care professionals may recommend bleach baths, which are analogous to chlorinated swimming pools, to decrease the need for systemic antibiotic use.[45] Parents or caregivers may create their own "swimming pool water," by adding 40 gallons of lukewarm water to a bathtub and a quarter to a half cup of common bleach. Allowing pediatric patients to soak in the tub for 5–10 minutes may decrease the number of skin infections children experience.[46]

A randomized, investigator-blinded, placebo-controlled trial enrolled 31 pediatric patients aged 2–17 years with moderate-to-severe atopic dermatitis.[47] Patients with signs of a skin infection received intermittent bleach baths or plain water baths (placebo). All of the patients received cephalexin 50 mg/kg/day for 14 days and intermittent mupirocin nasal ointment. Children were instructed to bathe in the bleach water for 5–10 minutes twice weekly for 3 months. The Eczema Area and Severity Index (EASI) was used to evaluate the head/neck, upper limbs, trunk, and lower limbs after 1 and 3 months of treatment. A significant difference in the EASI after 1 ($p = 0.03$) and 3 months ($p = 0.0005$) was observed when comparing the treatment arm to placebo arm, for sites that were submerged in the bath (ie, trunk, upper limbs, and lower limbs). In contrast, there was no difference in the EASI after 1 ($p = 0.32$) and 3 months ($p = 0.62$) of treatment for the site that was not submerged in the bath (ie, head/neck).

Summary

Pediatric patients with atopic dermatitis are encouraged to maintain a balanced diet and to avoid trigger factors such as allergens and irritants, which may include soaps, shampoos, detergents, and animal dander. Emollients are recommended for children with a diagnosis of atopic dermatitis regardless of symptoms. Pediatric patients can be started on a low-potency corticosteroid, such as hydrocortisone 1% or desonide 0.05%, and clinicians may advance to medium- or high-potency corticosteroids as needed, depending on the severity of the eczema. Calcineurin inhibitors may be an alternative in pediatric patients who are not responding or tolerating the adverse effects of corticosteroids or for those who have eczema located on the face or neck. Systemic corticosteroids are generally used as a last resort when topical agents have failed. Oral antihistamines may improve quality of sleep, but may not alleviate itching. Other treatment options that have been explored include phototherapy, bandages, and bleach baths. The effectiveness of phototherapy is uncertain and is contraindicated in children with a family history of skin cancer or very fair skin. Phototherapy may be considered when pediatric patients have failed other treatment modalities. There is no evidence to support the use of bandages; however, they may be useful in children who frequently scratch themselves by preventing further lichenification and exacerbation of atopic dermatitis. Studies have shown that bleach baths may reduce the severity of atopic dermatitis in children. Health-care professionals need to assess and consider the child's quality of life when determining which treatment is most appropriate.

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Table 7. Comparing Wet Wrap Therapy to Conventional Management of Pediatric Atopic Dermatitis[40]

Randomized Clinical Trial	Study Design	Results
Topical corticosteroids plus emollients vs topical corticosteroids plus wet wrap therapy	Children (N = 50) aged 4–27 mo were randomized to receive topical corticosteroids and emollients (conventional therapy) or wet wrap therapy in combination with topical corticosteroids; SCORAD index was used to assess patients' outcomes; 4 wk of therapy	Wet wrap treatment group had a 55% reduction in SCORAD score (24) compared to baseline (53); conventional treatment group had a 59% reduction (17) in score compared to baseline (41); no significant difference between groups ($p = 0.445$)

SCORAD = SCORing Atopic Dermatitis.

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