



What's new in the topical treatment of allergic skin diseases

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Purpose of review

To review recent literature on the topical treatment of allergic skin diseases to help clinicians make informed evidence-based decisions.

Recent findings

Twenty-four publications were identified from a *PubMed* search of randomized controlled trials and systematic reviews of topical treatment of atopic dermatitis and allergic contact dermatitis published from 1 January 2013 to 31 January 2014. Studies on the topical treatment of atopic dermatitis largely supported the recommended use of topical corticosteroids and topical calcineurin inhibitors. Barrier therapy continues to play an important role without evidence supporting use of one emollient over another. Lipoxin A4, an eicosanoid with anti-inflammatory properties, and a 5% cis-urocanic acid emulsion cream were effective in the treatment of atopic dermatitis, although studies were small. Adjunct therapy with bleach baths, natural oils, and textiles all showed some benefit; however, studies are limited. Literature on topical treatment of allergic contact dermatitis was limited to one publication, providing evidence for a natural multicomponent cream as maintenance therapy after control of disease with a topical corticosteroid.

Summary

There is strong evidence for the use of topical anti-inflammatory therapies in the treatment of atopic dermatitis. There is little evidence to suggest that one emollient is better than others.

Keywords

atopic dermatitis, contact dermatitis, topical calcineurin inhibitors, topical corticosteroids, topical therapy

INTRODUCTION

Allergic skin diseases are common and include atopic dermatitis, allergic contact dermatitis, and urticaria [1]. Although these diseases may have differences in their pathophysiology, and therefore may differ in their specific recommended treatments, overall, therapies focus primarily on reduction of inflammation and symptomatic relief of pruritus.

According to recent guidelines for the treatment of atopic dermatitis, topical corticosteroids remain the primary foundation of topical treatment, with topical calcineurin inhibitors (TCIs) preferred for treatment of the face and intertriginous areas [2]. Regular, liberal use of emollients is also recommended, and can have a steroid-sparing effect [3,4]. Recommended topical treatment of pruritus associated with atopic dermatitis also includes the use of topical corticosteroids, TCIs, and emollients [2]. Treatment considerations should include several factors, including age of the patient, severity of disease, and patient preference of therapy.

For allergic contact dermatitis (ACD) and urticaria, avoidance of the triggering allergen is key;

however, identifying specific triggers is often difficult. The topical treatment ACD is similar to that of atopic dermatitis, with topical corticosteroids the mainstay of therapy, along with the use of emollients [5]. There is some evidence from studies in nickel contact dermatitis that TCIs may be of benefit as well [6]. For urticaria, both acute and chronic, oral antihistamines are first-line therapy with no topical therapy recommended [7].

Familiarity with newer studies and treatment options help physicians make appropriate treatment recommendations. The objective of this study is to review recent research relevant to topical

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KEY POINTS

- Literature on the topical treatment of atopic dermatitis focuses largely on the use of topical corticosteroids and TCIs.
- Topical corticosteroids and TCIs are effective treatments for atopic dermatitis, with TCIs having the added benefit of improving skin barrier.
- Barrier therapy continues to play an important role in the treatment of atopic dermatitis.
- Adjunct therapies including bleach baths, natural oils, and textiles can be beneficial in the treatment of atopic dermatitis.

treatment of allergic skin diseases to help clinicians make informed evidence-based decisions.

METHODS

In order to identify recent studies regarding topical treatment of allergic skin diseases, a *PubMed* search was conducted using the Keywords: atopic dermatitis

treatment, allergic contact dermatitis treatment, and urticaria treatment. The search was limited to randomized controlled clinical trials and systematic reviews of topical treatment published from 1 January 2013 to 31 January 2014. This search yielded 305 results; and after the publications were reviewed for content, relevance, and duplicates, a total of 24 articles were selected (Fig. 1).

The studies were divided by disease, with atopic dermatitis further subdivided into anti-inflammatory agents, barrier therapy, natural oils, bleach baths, other topical agents, textiles, and factors associated with topical therapy. From each study, data on sample size, duration of study, dosage, efficacy, and adverse effects were reviewed.

RESULTS

Our literature search resulted in 23 publications on the topical treatment of atopic dermatitis, including 18 randomized clinical trials and five systematic reviews, and one publication, a randomized clinical trial, of topical treatment of allergic contact dermatitis. No publications were identified for the topical treatment of urticaria.

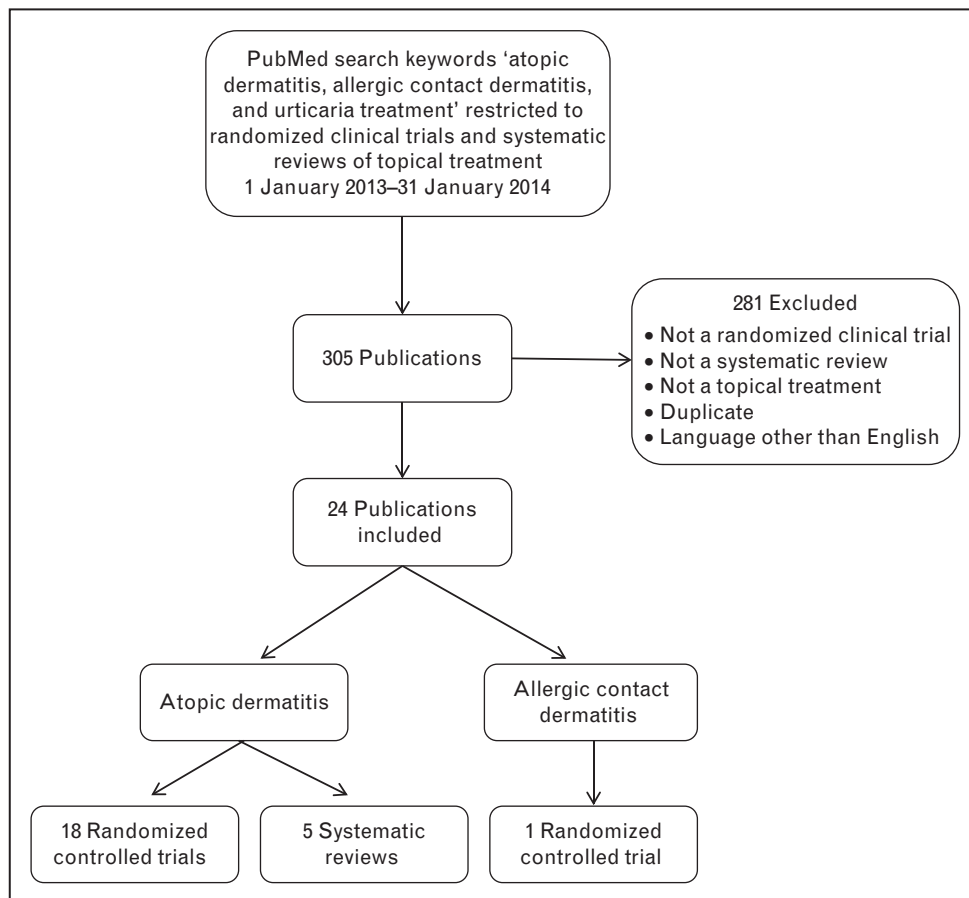


FIGURE 1. Flowchart of literature search.

Atopic dermatitis

Publications that met criteria for topical treatment of atopic dermatitis were further subdivided into the following: anti-inflammatory therapy, barrier therapy, natural oils, bleach baths, other topical therapies, textiles, and factors associated with topical therapy.

Anti-inflammatory therapy

Our literature search identified 10 publications regarding topical anti-inflammatory therapy of atopic dermatitis (Tables 1 and 2). Two studies compared a topical corticosteroid with a TCI. In a study by Danby *et al.* [8], topical betamethasone valerate and topical tacrolimus were compared in regard to their effects on skin barrier in patients with quiescent atopic dermatitis (history of atopic dermatitis with no symptoms for 6 months). Betamethasone valerate reduced both skin barrier function, bringing the transepidermal water loss (TEWL) closer to levels seen in patients with active atopic dermatitis, and skin hydration, whereas tacrolimus preserved skin barrier function and improved skin hydration. Tacrolimus also reduced skin pH and trypsin-like protease activity greater than treatment with the topical corticosteroid. Overall in patients with quiescent atopic dermatitis, betamethasone negatively impacted the condition of the skin, whereas tacrolimus improved the condition of the skin barrier. In patients with active atopic dermatitis, topical tacrolimus decreased TEWL and increased the lipid lamellae in the stratum corneum greater than mometasone furoate [9]. The TCI also doubled skin hydration, whereas the topical corticosteroid had no effect. Both were effective in terms of improvement in the SCORing Atopic Dermatitis (SCORAD). Another study by Jensen *et al.* [10] reported similar findings with the TCI topical pimecrolimus, which was superior at improving stratum corneum hydration and increasing the number of lamellar bodies when compared with the corticosteroid triamcinolone acetonide in patients with atopic dermatitis. The topical corticosteroid group, however, had better clinical improvement, achieving greater reduction in the partial Eczema Area and Severity Index (EASI) scores, lesion size, and pruritus. In contrast to the study by Danby, the topical corticosteroid improved TEWL more than the TCI. Overall, from a systematic review of 17 studies, TCIs and mild/moderate topical corticosteroids were reported to have comparable efficacy in treating atopic dermatitis and both were reported as being effective preventive treatment options [11]. Among the TCIs, tacrolimus 0.1% had greater efficacy than pimecrolimus 1% [11].

Another aspect of atopic dermatitis to consider when evaluating treatment options is pruritus. Topical tacrolimus was well tolerated and effective in treating refractory perianal pruritus according to itch, EASI, and Dermatology Life Quality Index scores compared with placebo [12]. Both topical corticosteroids and TCIs alike have demonstrated utility in treating pruritus [13]. A review suggested that topical corticosteroids were the most effective agents at reducing atopic dermatitis-related pruritus, and that the higher the potency of the steroid, the less itch occurred [13].

Vehicle choice can impact patient acceptance and adherence to treatment. Creams vs. ointments were compared in both children and adults, with patients preferring cream to ointment [14]. Pimecrolimus cream was reported preferred over tacrolimus ointment in terms of ease of use, quick absorption, lack of residue, and skin softness. Patients who used the pimecrolimus cream had better outcomes, according to the Investigator Global Assessment scale and reduction in affected body surface area.

Treatment regimens for administration of topical tacrolimus were also compared [15[¶]]. After twice daily application of tacrolimus 0.1% for 4 weeks, once weekly application of tacrolimus during a 40-week maintenance phase generated results comparable to that of thrice weekly application according to EASI scores, time to first relapse, and number of disease exacerbations.

Lipoxin A4 is an eicosanoid with anti-inflammatory properties. One study [16] explored the effectiveness of lipoxin A4 (LXA4) in treating infantile eczema. Patients using 15R/S methyl-LXA4 twice daily for 10 days had improvement on the EASI, severity scale score, and the Infants' Dermatology Quality of Life Index in a cohort of 20 patients, with efficacy comparable to mometasone furoate. Rates of relapse were similar between the two groups, 40 days after treatment.

Barrier therapy

Barrier therapy, consisting of creams and ointments, was studied in the treatment of atopic dermatitis, with seven publications resulting from our literature search. Hoppe *et al.* [17] explored the effects of three types of moisturizers in patients with atopic dermatitis with regard to filaggrin (FLG) mutation status. Moisturizers with propylene glycol, glycerol, and urea all improved dryness score at 4 weeks, with greatest improvement in patients with FLG—/— genotype. TEWL decreased with treatment as well in all groups, but was most reduced in the glycerol treatment group. None of the moisturizing therapies had an impact on filaggrin (*FLG*) gene expression in patients with mutations. Twice daily therapy with

Table 1. Topical treatment of atopic dermatitis: clinical trials

Study (total no. of patients)	Topical therapy	Duration	No. of patients	Age	SCORAD/EASI	TEWL	Other outcomes	Adverse effects	Authors evaluation of relevance ^a
Anti-inflammatory therapy									
Topical corticosteroids vs. calcineurin inhibitors									
Danby <i>et al.</i> [8] (n = 20)	Betamethasone valerate 0.1%	4 weeks bid	20	≥18		12.60–13.26	Decreased skin hydration by 3.8% and decreased natural moisturizing factors in SC	Not reported	(–)
Tacrolimus 0.1%									
						12.75–12.11	Improved skin hydration by 17%. Lowered pH and trypsin-like protease activity greater than with TC		+
Dahnhardt-Pfeiffer <i>et al.</i> [9] (n = 20)	Tacrolimus 0.1%	10 days bid	10	19–45	SCORAD: Between 10 and 63 to 0 and 20 (78% decrease)	–7	Increased skin hydration by double	Not reported	+
Mometasone furoate									
			10	19–48	SCORAD: Between 10 and 45 to 0 and 10 (83% decrease)	–4	No change in skin hydration	Not reported	+
Jensen <i>et al.</i> [10] (n = 15)	Triamcinolone acetonide cream 0.1%	22 days	15	21–45	EASI: Greater reduction in partial EASI with TC compared TCI		SC integrity improved from 64.0 to 54.3. Greater decrease in lesion size and pruritus than with TCI	Not reported	+
Pimecrolimus cream 1%									
							SC integrity improved from 64.0 to 52.7		(+)
Calcineurin inhibitors									
Ucak <i>et al.</i> [12] (n = 32)	Tacrolimus 0.03%	4 weeks bid	16	18–56	EASI: 1.7–0.72		After 4 weeks of treatment, DLQI decreased from 9 to 2.6. Itching score decreased from 3.75 to 1.68	Not reported	+

(Continued)

Table 1 (Continued)

Study (total no. of patients)	Topical therapy	Duration	No. of patients	Age	SCORAD/EASI	TEWL	Other outcomes	Adverse effects	Authors evaluation of relevance ^a
	Placebo (vaseline)		16		EASI: 1.8–1.67		After 4 weeks, DLQI decreased from 9.68 to 8.62. Litching score decreased from 3.81 to 3.62		
Onumah and Kirick [14] (n = 20)	Tacrolimus 0.1%	12 weeks	5	≥18			7% BSA reduction. 3.6 mean change in DLQI. 1-point improvement in IGA	Not reported	(+)
	Tacrolimus 0.03%		5	2–7					
	Pimecrolimus cream 1%		10	≥2			11.94% BSA reduction. 4.7 mean change in DLQI. 2.9-point improvement in IGA. Pimecrolimus cream was preferred to tacrolimus ointment		+
Chung <i>et al.</i> [15] (n = 142)	Tacrolimus 0.1%	Bid for 4 weeks, then three times weekly for 40 weeks	64	Not reported	EASI: Mean scores during maintenance phase similar between both groups		Time to relapse not significantly different between the groups, 110 days for once weekly application and 106 days for three times weekly	Burning, pruritus, and erythema reported with no difference between groups	+
		Bid for 4 weeks, then once weekly for 40 weeks	78						+
Eicosanoid									
Wu <i>et al.</i> [16] (n = 60)	15(R/S)-methyl-LXA4 0.1%	10 days bid	20	1–12 months	EASI: Significant reduction		Rate of eczema relapse was 63%. Significant reduction IDQOL	No AEs in any group. No changes in laboratory values	(+)

	Mometasone furoate cream 0.1%	10 days bid	20		Rate of eczema relapse was 53%. Overall, faster at improving Severity Scale Score compared with 15(R/S)-methyl-LXA4. Significant reduction IDQOL	+
Barrier therapy	Placebo cream	10 days bid	20	EASI: No significant reduction	No improvement in Severity Scale Score except in scaling	
	Glycerol 20% moisturizer	4 weeks	43	Not reported	Mean of all three groups 11.4–9.3. Most significant decrease with glycerol moisturizer, 12.3–9	No AEs
	Propylene glycol 20% moisturizer					
Urea 5% moisturizer	Emollient (glycerol + paraffin)	28 days bid	124	2–6	SCORAD: 3.21 reduction	Significantly greater reduction in xerosis score and xerosis VAS vs. vehicle. 66% of patients were responders in terms of xerosis score and SCORAD
						Mild or moderate erythema, burning, or pruritus in both groups. No severe AEs
Wanankul <i>et al.</i> [19] (n = 55)	Vehicle	28 days bid	125	2–6	SCORAD: 0.876 reduction	46% of patients were responders in terms of xerosis score and SCORAD
	Licochalcone A moisturizer	8 weeks bid	55	3 months–14	SCORAD: 26–14 at 4 weeks; 3 at 8 weeks	No AEs

(Continued)

Table 1 (Continued)

Study (total no. of patients)	Topical therapy	Duration	No. of patients	Age	SCORAD/EASI	TEWL	Other outcomes	Adverse effects	Authors evaluation of relevance ^a
Marini <i>et al.</i> [20] (n = 65)	Hydrocortisone cream 1%	4 weeks bid, followed by 4 weeks bid	65	18–65	SCORAD: 26–12 at 4 weeks; 3 at 8 weeks	27–26 at 22 at 8 weeks			+
	Ectoïne-containing moisturizer	28 days bid			SCORAD: 7.51–3.77. 28% patients had improvement between 50 and 75%		IGA decrease of 1.22, with 45% achieving clear or almost clear. Pruritus VAS decrease of 22.98 mm	Well tolerated with no differences between groups. Burning with both medications in one patient. Two local AEs with ectoine moisturizer and three with control	
	Positive control				SCORAD: 7.55–4.45. 35% patients had improvement between 50 and 75%		IGA decrease of 0.96, with 35% achieving clear or almost clear. Pruritus VAS decrease of 22.92 mm		
Simpson <i>et al.</i> [21] (n = 20)	Ceramide precursor-containing moisturizer	27 days bid	20	18–65		30% reduction from baseline	56% improvement in dryness. 118% improvement in SC hydration	No AEs	+
	Untreated control					4% reduction from baseline	22% improvement in dryness. 25% improvement in SC hydration		

Natural oils								
Danby <i>et al.</i> [23] (n = 19)	Olive oil	5 weeks bid	7	≥18	No difference between groups. After tape stripping, TEWL increased at treated site vs. untreated	SC 23% thinner on treated site vs. untreated	Not reported	–
Untreated control								
	Olive oil	4 weeks bid	12		9.89 g/m ² /h increase after tape stripping	SC thickness reduced by 0.988 ± 0.6418 μm	Mild erythema	–
	Sunflower seed oil				0.38 g/m ² /h decrease after tape stripping	SC thickness unchanged. Improved skin hydration by 12–18%	No AEs	(+)
Evangelista <i>et al.</i> [24] (n = 117)	Topical virgin coconut oil	8 weeks bid	59	1–13	SCORAD: 68.23% decrease	26.7–7.1 (70% decrease)	No AEs	(+)
	Mineral oil		58	1–13	SCORAD: 38.13% decrease	24.1–13.6 (35% decrease)	Increase in erythema, pruritus, or body surface area involved	(+)
Bleach baths								
Wong <i>et al.</i> [25] (n = 42)	Bleach baths 0.005%	2 months bid	21	2–30	EASI: Significantly greater reduction in treatment group vs. placebo	53% reduction in <i>S. aureus</i> density after 2 months. Greater reduction in BSA. Significant reduction in itch	Mild burning/stinging and dry skin in both groups	+
	Placebo		21	2–30		18% reduction in <i>S. aureus</i> density after 2 months		
Other topical therapies								
Peltonen <i>et al.</i> [26] (n = 45)	5% cis-urocanic acid emulsion cream	Once, then repeated 1 week later on DMSO-treated skin	16	18–45	cis-UCA decreased TEWL significantly more than control vehicle on day 10 and day 28	Erythema was decreased in both treatments	Tolerability of cis-UCA was comparable to control vehicle. There were no other significant AEs. No systemic absorption	(+)
Control vehicle								
(Continued)								

(Continued)

Table 1 (Continued)

Study (total no. of patients)	Topical therapy	Duration	No. of patients	Age	SCORAD/EASI	TEWL	Other outcomes	Adverse effects	Authors evaluation of relevance ^a
	5% cis-urocanic acid emulsion cream	10 days bid	16	18–65				Tolerability of cis-UCA was comparable to control vehicle, with mild erythema and formation of papules reported. There were no serious AEs and discontinuations	(–)
	Control vehicle								
	5% cis-urocanic acid emulsion cream	28 days bid	13	18–65	EASI: Significant improvement in both groups	cis-UCA decreased TEWL significantly more than control vehicle on day 10 and day 28	Significant decrease in erythema at day 10 and day 28	Most frequent treatment emergent skin-related AEs were pruritus and worsening of disease and were mild to moderate. No serious AEs or discontinuations	(+)
	Control vehicle						No significant decrease in erythema		
Textiles									
Araujo <i>et al.</i> [27] (n = 19)	Clothing made of cellulose fibers with seaweed enriched with silver ions	90 days	12	0–15	SCORAD: 45% reduction		70% reduction in pruritus VAS. 65% improvement in sleep quality	None	(+)
	Placebo cotton clothing	90 days	7		SCORAD: 42% reduction		60% reduction in pruritus VAS. 65% improvement in sleep quality	None	

Other topical treatment factors				
Futamura <i>et al.</i> [29 ^a] (n = 59)	Parental education	6 months	29	6 months–6
				SCORAD: 40.2–15.4
				Pruritus score declined from 5.5 to 1.6. Sleeplessness score declined from 4.6 to 1.3
				Not reported
				+
	Control group		30	SCORAD: 42.0–27.8
				Pruritus score declined from 6.5 to 3.8. Sleeplessness score declined from 4.7 to 3.0

Clinical trials of topical treatment of atopic dermatitis. AE, adverse effect; BSA, body surface area; cis-UCA, cis-urocanic acid; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; FCI, filaggrin; IDQOL, Infants' Dermatology Quality of Life Index; IGA, Investigator Global Assessment; SC, stratum corneum; SCORAD, SCORing Atopic Dermatitis; TC, topical corticosteroid; TCI, topical calcineurin inhibitor; TEWL, transepidermal water loss; VAS, visual analog scale.

^aFor authors' evaluation of relevance, + = strong recommendation for, (+) = weak recommendation against, and (–) = weak recommendation against.

an emollient containing glycerol and paraffin for 28 days in young children with atopic dermatitis resulted in significant improvement in xerosis score, xerosis visual analog scale (VAS), and SCORAD compared with vehicle [18]. More patients in the emollient group (66%) than the vehicle group (46%) were considered responders. In patients that relapsed after therapy was stopped, restarting emollient led to improvement similar to initial treatment.

The efficacy of a moisturizer containing 0.025% licochalcone A in a ceramide and linoleic lotion was compared with 1% hydrocortisone for the treatment of childhood atopic dermatitis [19]. Both treatments resulted in improvement on SCORAD; however, hydrocortisone was better at improving TEWL. Overall, moisturizers containing licochalcone can be beneficial in treating atopic dermatitis. In a separate study, a moisturizer containing ectoine had positive effects in adult atopic dermatitis patients and was well tolerated after 28 days of treatment. Marini *et al.* [20] reported that this ectoine-containing moisturizer had efficacy comparable to that of a positive control, a nonsteroidal anti-inflammatory cream, with no significant differences in improvement in SCORAD, Investigator Global Assessment, and pruritus VAS scores.

Two publications discussed the use of ceramide-containing moisturizers. A new moisturizer containing a ceramide precursor resulted in a significant improvement in TEWL, clinical dryness scores, and skin hydration after twice daily application for 27 days in adult patients with inactive atopic dermatitis [21]. Untreated control instead of a placebo was used in the study, limiting the ability to determine whether the improvement was a result of the pseudoceramide alone, the other active ingredients, or a combination of all the ingredients in the moisturizer. Recently developed moisturizers are now incorporating natural moisturizing factors, ceramides, and pseudoceramides, with some evidence of efficacy from a review of 33 studies on barrier therapy in atopic dermatitis [22^{aa}]. Findings from some of these studies were conflicting and inconsistent. Many of the trials had small sample sizes and did not assess all relevant parameters, making it difficult to draw conclusions regarding efficacy. The need for long-term studies was stressed.

Natural oils

Two publications in the literature explored the utility of natural oils in atopic dermatitis treatment. The first publication reported on two studies as follows: olive oil compared with no treatment for 5 weeks and olive oil compared with sunflower seed oil for 4 weeks, both in patients with and without atopic dermatitis. Olive oil decreased stratum

Table 2. Topical treatment of atopic dermatitis: systematic reviews

Study	Topical agents reviewed	Number of publications reviewed	Summary of findings
What's new in atopic eczema? An analysis of systematic reviews published in 2010–11 [11]	TCs, tacrolimus, pimecrolimus	24	TCIs or TCs are effective preventive treatment options for AD patients. Of the calcineurin inhibitors, tacrolimus 0.1% was found to be more efficacious than pimecrolimus 1%. Tacrolimus and mild/moderate TCs demonstrated similar efficacy
The effects of treatment on itch in atopic dermatitis [13]	TCs, TCIs, doxepin, menthol, cannabinoids	Not reported	The primary approach to pruritus in AD is anti-inflammatory treatment. TCs were the most effective agents at reducing itch. The higher the potency steroid the greater antipruritic effect. TCIs are also effective, less so than higher-potency TCs; however, data are limited. TCs should be used for control of disease and TCIs and intermittent TCs considered for maintenance
Barrier repair therapy in atopic dermatitis: an overview [22–24]	Barrier therapy: emollients and creams	13	Overall emollients, cream, and ointments improve the barrier function of the stratum corneum. Recently developed moisturizers are incorporating natural moisturizing factors, ceramides, and pseudoceramides, with some evidence of efficacy. The findings of research studies on these novel moisturizers seem to be conflicting and inconsistent
Functional textiles for atopic dermatitis: a systematic review and meta-analysis [28]	Functional textiles	13	Certain textiles such as silk textile and silver-coated cotton are safe and associated with some improvement in AD; however, because of low-quality evidence, the strength of the actual recommendation for textile use is weak
Timing of return office visit affects adherence to topical treatment in patients with AD: an analysis of five studies [30]	Adherence factors in topical treatment	5	Factors that most influenced high adherence rates were shorter treatment periods and follow-up visits scheduled shortly after starting treatment. Longer length of study resulted in worse adherence

Systematic reviews of topical treatment of atopic dermatitis. AD, atopic dermatitis; TC, topical corticosteroid; TCI, topical calcineurin inhibitor.

corneum thickness, with an increase in TEWL and caused mild erythema [23]. Patients with history of atopic dermatitis had a greater decrease in skin barrier function than patients without. Sunflower seed oil maintained skin barrier function and stratum corneum integrity and also increased skin hydration, with the greatest improvement in patients with history of atopic dermatitis. In another study [24], both coconut oil and mineral oil resulted in improvement according to SCORAD and TEWL. Coconut oil and mineral oil decreased SCORAD scores by 68.2 and 38.1%, respectively. In addition, coconut oil improved TEWL from a baseline of 26.7 to 7.1 and mineral oil reduced TEWL from 24.1 to 13.6. Although both oils demonstrated improvement, coconut oil had greater improvement of TEWL and SCORAD scores. The findings of both studies suggest that not all natural oils are equally beneficial to the skin, and olive oil, in particular, may be damaging to both normal and atopic dermatitis skin.

Bleach baths

In a study by Wong *et al.* [25], bleach baths were evaluated as an adjunctive treatment for atopic dermatitis; use of concurrent emollient and topical corticosteroid was allowed. Patients were instructed to soak in a bleach bath or placebo for 10 min twice daily for 2 months. These patients had greater improvement in EASI scores and BSA compared with placebo, and both groups reported reduced itch, with only the treatment group having a significant reduction in itch score at 2 months. Although the bleach baths resulted in a 53% reduction in *Staphylococcus aureus* colonization, there was no significant difference between treatment and placebo groups. A few patients in both groups experienced mild side-effects, including burning/stinging and dry skin.

Other topical therapies

Five-percent cis-urocanic acid (cis-UCA) emulsion cream was studied in adult patients with AD. In three separate studies, 5% cis-UCA tolerability was comparable with control vehicle [26]. cis-UCA applied twice daily for 28 days decreased TEWL and erythema significantly more than control vehicle at day 10 and day 28. Generalizability of these findings is limited because of a small sample size.

Textiles

Textile clothing has also been studied in atopic dermatitis management. Clothing made of cellulose fibers with silver ion-enriched seaweed improved SCORAD score, pruritus, and sleep quality; however, the improvement was not significantly different

from the control group which wore 100% cotton clothing [27]. A systematic review of 13 publications concluded that the various textiles used in the literature were safe and some were effective; however, because of the low-quality evidence, the strength of the recommendation for textile use is weak [28].

Factors associated with topical therapy

Parental education is an important aspect of atopic dermatitis management in children. A 2-day educational program for parents consisting of lectures, practical sessions, and group discussions was effective at decreasing atopic dermatitis severity at 6 months [29[¶]]. Patients of parents that received the educational program regarding proper topical corticosteroid and emollient application showed improvement in SCORAD and pruritus scores, and parents had less anxiety over using topical corticosteroids compared with the group that did not receive intervention [29[¶]].

Five studies that electronically measured patient adherence to topical corticosteroids for the treatment of atopic dermatitis were compared to determine factors that most influence compliance [30]. Higher adherence rates were associated with shorter treatment periods and shorter time between treatment initiation and follow-up visits.

Allergic contact dermatitis

Our literature search of topical treatment for ACD resulted in one publication (Table 3) [31]. This study [31] was specific to the treatment of vulvar dermatitis, including contact and allergic dermatitis. Patients were first treated with topical mometasone furoate 0.1% for 15 days or until they reached a VAS between 0 and 1, followed by treatment for 60 days with either a topical multicomponent cream containing anti-inflammatory and antiitching natural actives, including 18-beta glycyrrhetic acid, levomenol, zanthalene, curcumin, tea tree oil, and lactic acid, or placebo. Although both groups maintained a VAS less than 1, significantly fewer patients in the treatment group needed to use mometasone during this treatment period compared with the placebo group: seven vs. 42 patients, respectively (a total of 23 applications compared with 682 applications).

CONCLUSION

Standard of care for atopic dermatitis continues to be the use of topical therapy, with corticosteroids remaining first-line treatment when conservative measures fail. The literature from our review continues to support the use of these therapies, with research focusing largely on topical corticosteroids and calcineurin inhibitors. Several studies [8,10]

Table 3. Topical treatment of contact dermatitis

Topical therapy (total no. of patients)	No. of patients	Average age	Dose	VAS	Other outcomes	Adverse effects
Topical multicomponent cream [31] (n = 96)	18 contact dermatitis; 15 allergic dermatitis; 15 lichen simplex	57.9	MF 0.1% once daily × 15 days, then multicomponent cream once daily × 60 days	Baseline = 7.9; Day 15 = 0.4; Day 60 = 0.5	Seven patients needed to use MF during the multicomponent cream treatment phase, with a total of 23 applications	The majority of patients reported excellent tolerability. Burning reported in two patients in treatment group and one patient in placebo group, resulting in three total dropouts
	18 contact dermatitis; 14 allergic dermatitis; 16 lichen simplex	56.2	MF 0.1% once daily × 15 days, then placebo cream once daily × 60 days	Baseline = 7.6; Day 15 = 0.3; Day 60 = 0.8	42 patients needed to use MF during placebo phase, with a total of 682 applications	

Clinical trial of topical treatment of contact dermatitis. MF, mometasone furoate; VAS, visual analog scale.

compared these two therapies and reported that calcineurin inhibitors were as effective as steroids in treating atopic dermatitis, if not more in terms of improving the skin barrier. Although TCIs are especially useful for treatment of the face and intertriginous areas that are more prone to the adverse effects of topical corticosteroids, these studies indicate that TCIs may deserve a higher recommendation in the treatment of atopic dermatitis of the body. Although there is a Food and Drug Administration-issued black box warning on TCIs, several publications address the theoretical risk of malignancies and the lack of evidence behind these claims [32–34]. Because TCIs have an obvious benefit in the treatment of atopic dermatitis, physicians should be familiar with the facts concerning their safety in order to have educated discussions with patients. Similarly, patients need to be adequately educated on the safety of topical corticosteroids; this is especially important in that phobia of topical corticosteroids use has been cited as a barrier to treatment [35–37]. Topical corticosteroids vary in their potency and formulations, and generally there are several appropriate options to choose from depending on severity of disease, location being treated, and age of the patient. Some authors have suggested that some topical corticosteroids, such as mometasone furoate, have a better therapeutic index (fewer adverse effects with equivalence potency); however, there is no strong evidence to support this conclusion [38].

Barrier therapy continues to be a fundamental aspect of atopic dermatitis treatment; creams, ointments, and moisturizers are all potential treatment options for atopic dermatitis. Overall the literature does not contain any substantial evidence to support the use of one type of barrier therapy over another. There is a trend in newly developed moisturizers to contain substances, such as ceramides, pseudoceramides, and natural moisturizing factors, with some evidence for efficacy; however, the research findings on these novel moisturizers are inconsistent [21,22[■]].

The literature on natural oils suggests that certain natural oils may be beneficial in the treatment of atopic dermatitis. Sunflower seed oil, coconut oil, and mineral oil were all reported to have positive effects, whereas olive oil had negative effects on normal and atopic dermatitis skin [23,24].

Textile use in atopic dermatitis may be of some benefit; however, because of an overall low quality of evidence, recommendations cannot be made [28]. Bleach baths as adjunct therapy were effective at improving atopic dermatitis and reducing *S. aureus* colonization, supporting the current recommendation to include bleach baths in the treatment

regime for atopic dermatitis to help reduce microbial colonization and superinfections that can contribute to atopic dermatitis flares [2,25].

Strategies to improve patient adherence were another recurring theme in the literature. Futamura *et al.* [29[■]] emphasized the importance of parental education on topical steroid application, whereas Shah *et al.* [30] provided insight on strategies to improve adherence, such as early follow-up visits and shorter treatment durations. Patient preferences play a role in adherence; patients are more likely to use medications they prefer and, therefore, have improved treatment outcomes. Patients preferred pimecrolimus cream to tacrolimus ointment and had better outcomes with the cream; however, these results differ from Torley *et al.*'s [11] systematic review on TCIs that reported tacrolimus was more effective than pimecrolimus [14]. Simpler regimens including less frequent dosing schedules can also improve adherence, and given that once weekly application of tacrolimus was comparable to three times weekly, simpler regimens should be considered when appropriate [15[■]]. Providing patients with options and addressing other factors that may negatively impact adherence include steroid phobias and the black box warning on TCIs may also be of benefit.

Some populations of patients, including children and pregnant patients, deserve special consideration in the treatment of atopic dermatitis. Literature reviewed included infants and children and provided effective and safe treatment options [14,16,18,19,24,25,27]. Although pregnancy was not addressed, topical corticosteroids can be used safely in pregnancy [39–42]. Evidence-based guidelines recommend using the least potent topical corticosteroid necessary to control disease, with mild/moderate potency preferred over more potent topical corticosteroids [40]. TCIs are not recommended by the manufactures; however, their use for localized areas can be considered when topical corticosteroids or phototherapy are ineffective [41,42]. Use of barrier therapy is especially important in children and pregnancy and should be encouraged.

Literature on the topical treatment of ACD was limited, with one publication on the treatment of vulvar dermatitis. This study suggests that a natural multicomponent cream, with anti-inflammatory and antiitch properties, may be beneficial as maintenance therapy after control of disease first with topical corticosteroid treatment.

Overall, the literature continues to provide strong recommendations for anti-inflammatory and barrier therapies for the treatment of atopic dermatitis, whereas the evidence supporting other adjunct therapies, such as textiles, natural oils,

and bleach baths, remains limited. These adjunct therapies do provide the physician treatment options for patients seeking alternative therapies or who are fearful of potential risks of topical corticosteroids and TCIs. Ultimately, treatment regimens should be tailored to an individual's needs and preferences, keeping in mind evidence-based recommendations.

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Conflicts of interest

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