

JAMA Clinical Guidelines Synopsis

Management of Atopic Dermatitis

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GUIDELINE TITLE Guidelines of Care for the Management of Atopic Dermatitis: Management and Treatment of Atopic Dermatitis With Topical Therapies

DEVELOPER American Academy of Dermatology (AAD)

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PRIOR VERSION 2004

TARGET POPULATION Pediatric and adult patients with atopic dermatitis (AD) of all severities

MAJOR RECOMMENDATIONS

- Application of nonpharmacologic moisturizers is an integral component of the management of patients with AD,

resulting in reduced disease severity and a decrease in use of pharmacologic interventions (level of evidence I).

- Topical corticosteroids (TCSs) are an appropriate treatment of AD not controlled by moisturizers (level of evidence I).
- Topical calcineurin inhibitors (TCIs) are an important class of topical medication allowing for steroid-sparing interventions after achieving initial disease control with TCSs (level of evidence I). The data suggest that proactive regular, intermittent use of TCIs is additionally effective in maintaining disease remission (level of evidence I).
- Evidence suggests that bleach baths and intranasal mupirocin can decrease disease severity in those with moderate to severe AD and clinical signs of secondary bacterial infection (level of evidence II).

Summary of the Clinical Problem

Atopic dermatitis is a chronic inflammatory skin disorder affecting approximately 10% of US adults and children.^{1,2} The condition is the result of multiple factors including a hyperstimulated cutaneous immune system, a genetically determined compromised skin barrier, and exposure to triggering environmental stimuli. Flares manifest as extreme pruritus of red, rough, flaky and often fissured regions of the skin that become chronically thickened, rough, and discolored. Atopic dermatitis can have a profound effect on the quality of life of patients and their families through effects on sleep, behavior, mood, and absences from school and work.³ The topical therapies discussed in this guideline⁴ are considered the first line of management.

Characteristics of the Guideline Source

The guideline was developed by a panel of expert clinicians assembled by the AAD (Table). The panel reviewed the available data on the effectiveness of nonpharmacologic topical interventions for treatment of AD and the efficacy, optimal dose, frequency of application, and adverse effects of topical medications. The panel conducted a systematic review and developed recommendations from this evidence. In situations where evidence-based data were not available, expert opinion was used to generate clinical recommendations and identified as such within the text of the document, although not within all recommendation tables. The AAD manages conflicts of interest by prohibiting the funding of guideline production by outside entities, requiring detailed disclosures of all relevant relationships of guideline contributors, and recusing contributors when relationships are identified. Working groups are required to have a majority of participants with no relevant financial conflicts, and the chairman, medical writer, and affiliated staff may not have any relevant financial conflicts.

Evidence Base

A systematic search of the medical literature, Cochrane Library, and eczema trials databases resulted in review of 246 studies, including prior published guidelines on AD. The available evidence was evaluated according to the Strength of Recommendation Taxonomy.⁵

Among the nonpharmacologic practices considered, this review found that only use of moisturizers has been studied adequately in multiple randomized clinical trials (RCTs) to generate strong evidence in favor of a benefit. The optimal moisturizer vehicle (ointment, cream, lotion, gel, oil), the quantity to be applied, and the frequency of application has not been systematically studied. A new class of moisturizers known as prescription emollient devices has emerged. These agents are approved as medical devices and not drugs and are therefore not subject to rigorous efficacy review by the US Food and Drug Administration. The manufacturers claim that their products target the defects in the skin barrier that have been observed in AD. The evidence base to support their benefit above other moisturizers in controlling AD is currently weak.

Table. Guideline Rating

Standard	Rating
1. Establishing transparency	Good
2. Management of conflicts of interest in the guideline development group	Fair
3. Guideline development group composition	Poor
4. Clinical practice guideline-systematic review intersection	Good
5. Establishing evidence and rating strength for each of the guideline recommendations	Good
6. Articulation of recommendations	Good
7. External review	Fair
8. Updating	Good
9. Implementation issues	Good

The published evidence is not robust enough to determine best bathing practices; thus, only expert clinical consensus opinion is provided. Use of non-soap-based surfactants and synthetic detergents are recommended (agents with a pH closer to that of normal skin); evidence does not exist to support use of water-softening devices, bath water additives, or acidic water. Use of bleach in bath water in combination with intranasal mupirocin vs plain-water baths was studied in 1 RCT of children with moderate to severe AD and clinical signs of secondary bacterial infection and demonstrated improvement in disease severity.⁶ This practice is recommended as potentially beneficial but requires further study.

The benefits of TCSs in AD have been demonstrated in numerous RCTs, making them the first-line recommended therapy when nonpharmacologic measures have failed. The confirmed benefits are reducing acute and chronic signs of AD and reducing itch associated with AD. Comparative trials of different TCSs are uncommon; therefore, data are not available to support any specific TCS over another. Patient vehicle preference, cost, availability, and lesion location typically guide agent and potency selection. There is limited evidence guiding how to dose TCSs based on agent potency or the optimal frequency of application. There is no universal standard for quantity of application or body surface area to weight ratio adjustments. The authors note that early data suggest that proactive maintenance use of a TCS on sites of frequent flares of AD may be effective at preventing relapses.

Topical calcineurin inhibitors are another class of anti-inflammatory agents that has been shown to be effective in the management of AD in short- and long-term vehicle-controlled trials. A meta-analysis of 25 RCTs found tacrolimus to be as effective as mid-potency TCSs, whereas pimecrolimus is less efficacious than mid- and high-potency TCSs.⁷ Topical calcineurin inhibitors are thus recommended as steroid-sparing agents in the treatment of AD. Topical calcineurin inhibitors have the benefit of not causing cutaneous atrophy and therefore are of particular utility at sites of thin or sensitive skin. Similar to recent findings related to maintenance use of TCSs to prevent flares, proactive, intermittent application of TCIs to recurrent sites of AD is recommended to reduce relapses. Comparative data do not strongly indicate a definite benefit of one TCI over another. There are limited data regarding a benefit to use of TCIs in combination with TCSs, either sequentially or concomitantly.

Wet wrap therapy, variably incorporating the use of topical medications, moisturizers, or both, is a method often recommended to

manage significant flares of AD or recalcitrant disease; however, rigorous trials of best technique are lacking.

Benefits and Harms

Benefits of topical therapy for the management of AD include improvement in the symptoms of an often morbid disease while avoiding the risks of systemic therapy. Use of moisturizers avoids exposure to any pharmacologic agent.

The clinical challenge of using nonpharmacologic interventions is that these therapies require continued regular use and an acceptance by the patient of the sensation of the agent on the skin. Additionally, patients with AD are at increased risk of irritant and allergic contact dermatitis precipitated by topical exposures; therefore, care must be taken in choosing products with a low risk of sensitization and caregivers must be alert to the possibility of coexistent contact dermatitis.

Anxiety exists among patients, caregivers, and physicians about the use of TCSs.⁸ Although local cutaneous adverse effects and risks related to systemic absorption may need to be considered, systematic reviews have concluded that TCSs have a good safety profile.⁹ No specific monitoring for systemic adverse effects is recommended for patients with AD. Patients and caregivers should be counseled carefully regarding the true risks and benefits to achieve a therapeutic alliance. The most common adverse effect of TCI use is local burning or stinging, which generally improves after several applications. Thus, patients should be advised of this effect to avoid premature discontinuation.

Discussion

Successful management of AD improves patient quality of life. The available evidence supports treatment's positive effect on the wide-ranging symptoms of AD, including irritability, sleep disturbance, itching, pain, disfigurement, embarrassment, depression, and isolation. The biggest challenge is to avoid undertreatment by achieving adherence to task- and time-intensive regimens of skin-directed care.

Areas in Need of Future Study or Ongoing Research

The authors of this guideline indicate significant gaps in the evidence related to topical therapies for AD. Specifically needed are RCTs to better determine optimal bathing techniques, including the generalizability of the benefits of bleach baths. Well-designed, large trials to better test the effects of topical antimicrobial agents and TCS-TCI combinations and studies to provide additional long-term safety data on the use of TCIs are needed.

ARTICLE INFORMATION

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