Long-Term Treatment of Atopic Dermatitis

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KEYWORDS

• Long-term • Atopic dermatitis • Eczema • Treatment • Topical therapy • Systemic therapy

KEY POINTS

- Proactive, twice weekly therapy with either a topical corticosteroid or topical calcineurin inhibitor can decrease frequency of flares in patients with moderate to severe disease.
- The long-term efficacy and safety of current systemic treatments for atopic dermatitis is poorly studied and comparative trials are low powered; newer, safer alternatives are needed.
- Cyclosporine is the second-line agent with the most evidence of efficacy, and phototherapy is likely the safest.
- Methotrexate or mycophenolate mofetil/sodium may be as efficacious as cyclosporine for long-term use with potentially fewer side effects.
- Additional evidence is required before a definitive recommendation can be made.

INTRODUCTION

Atopic dermatitis (AD) is a common inflammatory systemic disease characterized by eczematous skin lesions and pruritus, and frequently accompanied by a host of other allergic disorders that manifest in the upper or lower airways, eyes, and/or the gastrointestinal tract. Therefore, the ideal, long-term management of AD may need to address both the cutaneous and systemic inflammation that is present in the circulation and even in distant organs. There is little consensus on what constitutes "long-term" treatment for chronic, inflammatory diseases. For example, in rheumatoid arthritis, long-term treatment has been defined as 1 year or longer.[1] In contrast, 12 weeks has been referred to as "long-term" in AD literature, which may simply reflect the paucity of interventional randomized, controlled trials (RCTs) greater than 3 months in duration.[2]

Outcome measures in the trials vary widely, making direct comparisons between trials and consequently between treatments or treatment regimens difficult. This literature uses terms such as remission, relapse, flare, and rebound, but how these terms are defined is not always clear or consistent.[3] Fortunately, the Harmonizing Outcome Measures for Eczema group is working toward standardizing outcome measures so trial comparisons in the future may be more accurate and informative (**Box 1**).[4]

METHOD

RCTs of 12 weeks or longer were identified by a Pubmed search for terms "atopic dermatitis," "atopic eczema," and "long-term" along with a review of the Global Resource of Eczema Trials database (greatdatabase.org.uk), consensus papers, and systematic reviews.[5–7] Repeated short

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Box 1
What is meant by an AD flare (relapse)?

- There is no consensus on the definition.
  - Thirty-five percent of trials in a recent review used an arbitrary cutoff (eg, Investigators Global Assessment >4).[3]
  - Twenty-three percent of trials used the need to step-up treatment, in the physicians or patients opinion.[3]
  - The remainder used a composite or had no relapse definition.[3]
  - Nonflared AD is referred to stabilized AD or in "remission."

Abbreviation: AD, atopic dermatitis.

courses of treatment were included as long as the cumulative treatment period was at least 12 weeks. Trials not searchable by Pubmed were excluded. Only trials with a primary outcome of treatment efficacy or safety were included. Trials were excluded if information deemed necessary were missing (eg, study population ages or duration of treatment).

BATHING

Bathing can hydrate the skin while promoting the removal of irritants and allergens.[6] Expert consensus recommends up to once daily bathing, for a short period of time with lukewarm water.[6] Application of a moisturizer or a topical antiinflammatory agent immediately after bathing, often referred to as the "soak and smear" technique, is strongly encouraged (**Box 2**).[6]

Cleanser composition and pH affect skin barrier structure and function.[6] Normal skin has a slightly acidic pH (pH 4–5.5).[6] Soap, which typically has an alkaline pH, is thought to have detrimental effects on stratum corneum proteins and lipids.[6] Although there are no long-term RCTs evaluating cleansers, an acidic or neutral, nonsoap cleanser (eg, synthetic detergent [Syndet]) should be recommended to AD patients.[6]

Box 2
What is the literature[a] lacking?

- Optimal frequency or duration of bathing.
- Efficacy of the soak and smear technique.
- Optimal cleanser composition.
- Efficacy of bath additives (eg, oatmeal, Epsom salts, vinegar, or essential oils).
- Efficacy of water softeners.
- Comparison of soap versus synthetic detergents (Syndets).

[a] Long-term randomized, controlled trials in patients with atopic dermatitis.

Sodium Hypochlorite (Bleach) Baths and Antiseptics

Only 1 small, long-term RCT found that twice weekly bleach baths (along with 7 d/mo of intranasal mupirocin) had a significant reduction in eczema area and severity index (EASI) and body surface area (BSA) affected (**Table 1**). These pediatric patients were randomized after an episode of clinically infected AD treated with 2 weeks of oral cephalexin.[8] Compliance was similar between the groups. Surprisingly, bleach baths did not affect *Staphylococcus aureus* skin colonization as measured by standard culture techniques (**Box 3**).[8]

Box 3
What is the literature[a] lacking?

- Efficacy and safety of sodium hypochlorite (bleach) baths as a monotherapy.
- Relative efficacy of bleach baths in patients noncolonized versus patients with colonized/infected AD.
- When and how to use mupirocin or other topical or systemic antibacterials.
- Efficacy of antibacterial clothing (eg, silver-coated textiles).

[a] Long-term randomized, controlled trials in patients with atopic dermatitis.

MOISTURIZERS

Topical moisturizers contain variable amounts of emollient, occlusive, and humectant ingredients aimed at reversing the generalized xerosis and enhancing the barrier function measured by transepidermal water loss.[6]

One long-term trial found twice daily moisturization decreased the median time to relapse from 30 to more than 180 days compared with no moisturization.[26] In a long-term RCT in adults, moisturization with a 5% urea-based moisturizer decreased the risk of AD relapse by 37% versus a cream without urea (see **Table 1**).[9]

Several prescription emollient devices have received approval as medical devices: EpiCeram, Atopiclair, Mimyx, HylatopicPlus, Tetrix, Tropazone, Neosalus, Zenieva, Neosalus, and Eletone.