Summary

Emollient treatment of atopic dermatitis: latest evidence and clinical considerations

Hon KL, Kung JSC, Ng WGG, Leung TF. Drugs in Context 2018; 7: 212530. DOI: 10.7573/dic.212530

Introduction

- Atopic dermatitis (AD) is an inflammatory skin disorder with varying degrees of inflammation, erythema and dryness. It may be complicated by staphylococcal infection. The primary symptoms of AD are pruritus and sleep disturbance, affecting quality of life.
- The mainstay of treatment for AD is regular use of emollients and topical medications.
- Emollients are complex mixtures of chemical agents designed to soften the epidermis and make it more pliable. They provide an occlusive barrier to retain moisture and protect the skin from irritants. Advances in the understanding of the pathophysiology of AD has led to production of new moisturisers targeted to replenish ceramides and natural moisturising factors in the stratum corneum and there are numerous formulations claiming to have antimicrobial, antipruritic and anti-inflammatory actions. It is also common to find other herbal/animal-derived active ingredients added into commercial emollients, which claim to have beneficial effects on the skin. However, not all of these products have been subject to clinical studies to prove clinical efficacy.
- Selecting an appropriate emollient for treatment of AD is critical. Some contain allergens (e.g., fragrances and tocopherol) and eczematous skin may be prone to secondary sensitisation with frequent application of some emollients.

Components of emollient products

- The major ingredients of different emollient products are similar, consisting of petrolatum, paraffin, glycerine, plant-derived butter and oils in different combinations.
- **Occlusive agents** include lanolin, mineral oils, olive oil, petrolatum ceramide, paraffin and silicone. They are similar to the intercellular lipid bilayers of ceramide, cholesterol and free fatty acids, forming a thin hydrophobic film on the surface of the skin to retard loss of moisture across the epidermis.
- **Humectants**, such as glycerine, alpha hydroxyl acids and sorbitol, attract water vapour to moisturise the skin in the same way as the natural factors in the corneocytes.
- **Emollients**, such as collagen, elastin, glyceryl stearate and shea butter fill cracks between desquamating corneocytes and smooth the skin.
- An ideal emollient should contain a combination of occlusive agents to slow down water loss, humectants to increase capacity to withhold moisture and lubricants to reduce friction against skin.

1. Aqueous cream

- Aqueous cream (AC) is one of the most commonly used emollients. However, in comparison to other emollients, users have measurably lower skin hydration and it is less well accepted by consumers.
- AC products may contain sodium lauryl sulfate (SLS), which can cause skin irritation.
- Chronic use of AC has been reported to reduce stratum corneum thickness in increase transepidermal water loss. Furthermore, treatment with AC is associated with desquamatory and inflammatory protease activity.
• AC BP should not be used as a leave-on therapy for AD.

2. Plant derived products

2.1 Aloe vera
Aloe vera is a succulent plant commonly used in the skin-care industry. It possesses moisturising, antibacterial and antifungal actions, which might be helpful to prevent secondary infection in patients with AD. However, although it has been studied in patients with gastrointestinal conditions and diabetes, there are no controlled trials of aloe vera in patients with AD. Animal studies have shown variable results, including reductions in serum markers of inflammation.

2.2 Coconut oil
Coconut oil is commonly added to emollient preparations. However, it is important to specify whether the ingredient used is coconut oil or virgin coconut oil (VCO), since they have significantly different properties. VCO is claimed that it is superior to coconut oil because, in contrast to coconut oil, the active components, such as fatty acids, are retained during preparation. Although there are limited clinical trials to support this claim, VCO has been shown to significantly reduce severity of eczema and, in some studies, but not all, to have antibacterial effects, including against S. aureus. Antibacterial effects are attributed to the combined action of medium-chain fatty acids and monoglycerides, which disrupt the bacterial plasma membrane.

3. Animal products

3.1 Lanolin (wool grease/wool wax)
Lanolin is an occlusive agent produced from the sebaceous glands of sheep. There are different derivatives of lanolin in various emollient products, but there are few studies on the effects of lanolin in AD. Lanolin has been associated with contact allergy and daily application should be avoided in patients with AD.

3.2 Horse oil
Horse oil is a common ingredient in cosmetic products in Asian countries. It is claimed to have antibacterial, anti-inflammatory and antipruritic actions on the skin. The validity of these claims is unknown.

4. Special ingredients

4.1 Ceramides
Ceramides are lipid molecules found in naturally high concentrations within cell membranes of cells in the stratum corneum, which function to maintain the integrity of the skin barrier and prevent water loss. In comparison to healthy skin, ceramide levels are lower in the skin of patients with AD. Studies of emollients containing ceramide/ceramide-precursors in patients with AD have demonstrated variable results. These include improvement in SCORAD (SCORing Atopic Dermatitis, a clinical tool for objectively assessing the severity of atopic dermatitis), reduced transepidermal water loss and increased skin hydration. Newer moisturisers may include pseudoceramides. These are commercially synthesised ingredients that are claimed to possess anti-inflammatory properties and improve skin permeability and antimicrobial barrier function.
4.2 Natural moisturising factors
Natural moisturising factors (NMFs) are water-soluble filaggrin-degradation products that maintain hydration of the superficial layers of the stratum corneum by absorbing water from the atmosphere. They include urea, pyrrolidone carboxylic acid, glutamic acid and other amino acids, and are responsible for aggregating keratin filaments to form keratin bundles that maintain the rigid structure of the cells in the stratum corneum. Loss of NMF is prevented by the intercellular lipid layer which seals the outside of each corneocyte. In a small cohort study, an emollient containing 5% urea (NMF), ceramide NP and lactate was shown to provide more effective and sustained skin hydration than a control emollient.

4.3 Antimicrobial peptides
Antimicrobial peptides (AMPs) are components of the innate immune response. They have potent, broad spectrum antimicrobial activities against Gram-negative and Gram positive organisms, enveloped viruses and fungi, and activity against transformed malignant cells. They may enhance immunity by acting as immunomodulators. There are no studies to validate the efficacy of these agents in emollient preparations.

4.4 Ectoin
Ectoin is an organic osmolyte that can be isolated from a wide range of halophilic and halotolerant bacteria that live in extreme conditions. It is an osmoprotectant that increases bacterial resistance to hydration. Emollients containing ectoin have been developed to reduce water loss from dry skin of patients with AD. Trials have demonstrated significant reduction in the clinical severity of AD.

Review of clinical studies
The mean duration of studies on emollients was 6.7 weeks and the mean age of patients was 18.6 years. Most studies compared emollient to vehicle or no treatment. Overall, in comparison to control, most moisturisers/emollients showed some beneficial effects with no demonstrable difference between the different products:
1. Patient rating: subjective improvement in eczema and symptoms of itch vs. control;
2. Investigator rating: reduced disease severity and flares vs. placebo, vehicle or no moisturiser.
3. Prolonged time to flare, reduced number of flares and reduced amount of topical corticosteroids needed to achieve similar reductions in eczema severity.
Combining moisturisers with active topical treatment was more effective than active topical treatment alone.

Doctors remain the most important source of recommendation of moisturisers/emollients. The majority of patients believe that the ideal moisturiser is nonfragrant, nonherbal, white or transparent cream that needs to be applied only two or three times a day. Compliance is enhanced if the recommended moisturiser confirms to the parent’s/patient’s preference.