VIEWPOINT OPEN ACCESS

Clinical Benefits of Basic Emollient Therapy for the Management of Patients With Xerosis Cutis

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ABSTRACT

Xerosis cutis refers to dry skin that may be caused or exacerbated by external triggers (e.g., cold weather), endogenous factors (e.g., aging), or present as a symptom of other diseases (e.g., atopic dermatitis). Emollients are topical products formulated to rehydrate and restore the barrier function of the skin and are consistently recommended for the management of xerosis cutis and related diseases. Following the previous articles in this supplement, the present article aims to review the wider spectrum of clinical benefits associated with emollient therapy for xerosis cutis and diseases associated with dry skin. In clinical studies, the biophysical effects of emollients are often demonstrated using instrumental measures of skin hydration and barrier function, as well as clinical scoring systems that grade xerosis severity. In addition to these objective measures, the effectiveness of emollients has also been assessed by evaluating changes in subjective symptoms and patient-reported quality of life. Other reported benefits of emollient therapy for atopic dermatitis include delaying and preventing flares and reducing topical corticosteroid use. Although the current body of literature demonstrates the wide range of clinical benefits of emollient therapy for xerosis cutis, they also highlight a high degree of heterogeneity across clinical studies, a need for consensus outcome measures that facilitate direct comparisons between formulations, and a need to establish treatment targets for emollient therapy in clinical practice. Nevertheless, available evidence indicates that emollients demonstrate a favorable risk–benefit profile overall and should continue to be the mainstay of basic therapy for people with xerosis cutis and diseases associated with dry skin.

1 | Introduction

Regular emollient therapy is a well-established strategy for managing xerosis cutis (dry skin) and related diseases, including atopic dermatitis (AD), psoriasis, ichthyosis, senile xerosis, and diabetic foot disease [1–8]. Several systematic reviews have highlighted the large body of clinical evidence to support emollient therapy in patients with xerosis cutis [9–13]; however, they also show that direct comparisons between products are difficult to draw due to substantial heterogeneity across clinical studies. Sources of heterogeneity include differences in study design and the formulation of the emollient because the composition of an "inert" vehicle will influence the bioavailability and physicochemical effects of the "active" compounds that it carries [14, 15].

In addition, the previous articles within this supplement have shown that emollient studies vary widely with respect to outcome measures, which include instrumental measures of biophysical parameters and clinical scoring systems that grade objective signs of xerosis cutis [16, 17]. This present article

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Summary

- Why was the study undertaken?
  - This article aims to review the wider spectrum of clinical benefits associated with basic emollient therapy for xerosis cutis and diseases associated with dry skin.
- What does this study add?
  - In addition to objective measures of xerosis severity, clinical studies have shown that basic emollients can improve subjective symptoms (e.g., pruritus) and patient quality of life and reduce flares and corticosteroid use in those with atopic dermatitis.
- What are the implications of this study for disease understanding and/or clinical care?
  - Current evidence reinforces that most emollients are safe and effective treatment options for patients with xerosis cutis. However, it also highlights the need to establish consensus outcome measures and treat-to-target strategies for future research and clinical practice.

aims to review the wider spectrum of clinical benefits associated with emollient therapy for xerosis cutis and discuss how these might be incorporated into treatment strategies that improve the long-term management of patients with xerotic skin conditions.

2 | Effect of Emollients on Different Measures of Xerosis Severity

Xerosis cutis is a burdensome dermatological condition characterized by rough, scaly, and often itchy skin [1, 2]. Xerosis cutis may occur in response to external triggers (e.g., cold weather, frequent washing) or endogenous factors (e.g., aging, hormonal changes, genetic predisposition) or present as a symptom of other diseases (e.g., AD, psoriasis, diabetes mellitus). Regardless of the underlying cause, the primary goal of emollient therapy for xerosis is to rehydrate the stratum corneum (SC) and restore the barrier function of the skin. This is traditionally achieved with products formulated with ingredients that bind and hold water in the skin (e.g., glycerol, urea, lactic acid), replenish the intercellular matrix of the SC (e.g., ceramides, cholesterol), and create an external film to prevent evaporative water loss (e.g., liquid paraffin, petrolatum) [1, 18].

In clinical studies, the effects of emollients on dry skin can be objectively measured using corneometry (which measures skin capacitance or hydration) and evaporimetry (which measures transepidermal water loss [TEWL]) [1]. Other instrumental measures of emollient effectiveness include profilometry to visually examine skin topography and spectroscopy to evaluate SC lipid composition and structure [1, 19]. However, emollient studies should also include outcome measures that elucidate how changes in biophysical parameters translate to improvements in the signs and symptoms of xerosis cutis. For example, in a phase 3 study of a glycerol-liquid paraffin/petrolatum emollient (Dexeryl) in children with AD, treatment was associated with improvements in SCORing of Atopic Dermatitis (SCORAD) xerosis scores that coincided with improvements in skin hydration measured using a corneometer [20]. Other studies of this glycerol-liquid paraffin/petrolatum emollient have similarly shown that it can improve xerosis severity as measured by the Scaling Roughness Redness Cracks (SRRC) score in patients with ichthyosis [21] and the Xerosis Assessment Score (XAS) in patients with diabetes and foot xerosis [22]. However, a systematic review of emollients for foot xerosis noted the wide range of scoring systems used across clinical studies (including *ad hoc* scoring methods developed by investigators) [10], thus highlighting the need for consensus and consistent use of validated outcomes to facilitate product comparisons.

3 | Effect of Emollients on Patient-Reported Symptoms and Quality of Life

In addition to objective measures of xerosis severity, several studies have demonstrated the benefits of emollient therapy on subjective symptoms (e.g., pruritus) and patient quality of life. For example, these benefits were reported in an intra-individual study of the same glycerol-liquid paraffin/petrolatum emollient described above in 100 patients with uremic xerosis [23]. Patients applied the test emollient and comparator (vehicle without glycerol and liquid paraffin/petrolatum) to the left and right lower legs twice daily during a 7-day double-blind period, then entered an open-label treatment period through day 56 [23]. Over 8 weeks of treatment, the test emollient was associated with significant reductions in the severity of patient-assessed pruritus and substantial improvements in quality of life measured using the Short Form-12 questionnaire and Dermatology Life Quality Index (DLQI) [23].

Similarly, an open-label study by Cristaudo and colleagues evaluated the effect of the glycerol-liquid paraffin/petrolatum emollient on instrumental, clinical, and subjective measures of treatment response in 50 patients with AD [24]. After 60 days of twice-daily application, emollient therapy was associated with significant improvements in biophysical parameters (TEWL and skin hydration), which coincided with significant improvements in disease severity (measured by SCORAD index and four-point scales for xerosis, fissuring, itching, and erythema) and patient quality of life (measured by DLQI) [24]. Several other studies have shown that remoisturising and restoring skin barrier function with various emollients can improve subjective symptoms and quality of life in patients and caregivers of those with xerotic skin conditions [25–31].

4 | Other Clinical Benefits of Emollients in Atopic Dermatitis

In the field of AD, other reported benefits of emollient therapy include the primary prevention of AD, the secondary prevention of flares, and reductions in corticosteroid use. Based on the hypothesis that improving skin barrier function from infancy may prevent the development of AD, several studies have investigated whether early emollient use may be an effective strategy for primary AD prevention. While some earlier studies suggested that regular emollient use in infants may

be associated with reduced incidence and risk of developing AD [32–35], results from subsequent trials do not support emollient therapy as a primary prevention strategy [36, 37]. Indeed, a recent Cochrane review of skin care interventions during infancy concluded that emollient use during the first year of life is probably ineffective at preventing eczema and may conversely increase the risks of skin infection and food allergy in these infants [38]. However, the authors of another meta-analysis suggest that emollients may delay rather than prevent AD and that the efficacy of prophylactic emollient use may depend on the infant's risk for developing AD, age, and treatment duration [39].

Nevertheless, a separate Cochrane review of emollient and moisturizer use in patients with AD found that most formulations are beneficial for secondary prevention as they reduce and delay the incidence of flares and the amount of topical corticosteroid needed to improve eczema severity [9]. These benefits were demonstrated in a randomized, open-label study that compared the glycerol-liquid paraffin/petrolatum emollient (Dexeryl), a reference emollient (Atopiclair), and no treatment in 335 children with AD [40, 41]. In this study, patients with a current AD flare were treated with a topical corticosteroid (0.1% desonide) until resolution, then randomized to apply the glycerol-liquid paraffin/petrolatum emollient twice daily, the reference emollient three times daily, or no treatment for 12 weeks [40, 41]. Compared with no treatment, both emollients (particularly the glycerol-liquid paraffin/petrolatum formulation) were associated with a significantly reduced incidence of AD flares, delayed time to first flare, reduced corticosteroid or immunosuppressant use, and improved xerosis and AD severity scores over the treatment period. Other studies have consistently demonstrated the steroid-sparing and flare-reducing effects of an emollient therapy in patients with AD [42–51], highlighting that such benefits are achievable across a wide range of formulations.

5 | Risk–Benefit Evaluation of Emollients for Xerosis Cutis

In addition to the wide range of benefits described in this review and other articles within this supplement [16, 17, 52], the risks of emollient therapy for xerosis cutis are overall low. Like efficacy outcomes, adverse events (AEs) associated with emollients are inconsistently reported in the literature; however, available evidence suggests that they are typically skin-related (e.g., contact allergy, folliculitis), generally uncommon, and usually mild. For example, a recent literature review concluded that emollients are generally safe for use in AD; the incidence of treatment-related AEs ranged between 2% and 59% across clinical studies, with no serious treatment-related AEs reported [53]. Similarly, a Cochrane review of emollient use in AD estimated that the risk of AEs with any emollient formulation (24 per 100 participants) was not significantly different than with placebo, vehicle, or no emollient (23 per 100 participants; relative risk [95% CI], 1.03 [0.82–1.30]) [9]. The use of emollients on infant skin may have additional safety considerations, such as increased risk of irritation with some ingredients (e.g., haptens) [54], increased susceptibility to bacterial or fungal infection with contaminated products [55], and increased risk of systemic absorption due to the unique structure of infant skin and their increased surface area to volume ratio [56]. Providing patients and caregivers with instructions on the proper use and storage of emollients is therefore essential. Additionally, patient organizations and institutions, such as the European Academy of Dermatology and Venereology (EADV), provide online resources for patients with guidance on optimal emollient use [57]. Overall, emollient therapy demonstrates a favorable risk–benefit profile for people with xerosis cutis and diseases associated with dry skin, reinforcing its place in the treatment pathway for these conditions.

6 | Treat-To-Target Strategies for the Management of Xerosis Cutis

Despite the well-established efficacy and safety of emollients for xerosis cutis, poor adherence has been identified as a key barrier to achieving optimal outcomes with topical dermatological therapies [1, 58, 59]. Potential reasons for, and strategies to address, low adherence to emollient therapy are discussed in the following article within this supplement [52]; however, adopting a treat-to-target (T2T) approach in clinical practice may improve the long-term management of xerosis cutis and diseases associated with dry skin. T2T is a pragmatic, shared decision-making strategy that involves establishing “treatable traits” of the disease, setting measurable treatment targets for these traits, and choosing to continue, discontinue, or modify therapy until treatment targets are met [60, 61].

T2T strategies are commonly used to manage rheumatoid arthritis and other chronic diseases and are increasingly being developed in the field of dermatology [60, 61]. Most studies to date have sought to achieve consensus on treatable traits and associated treatment targets to guide systemic therapy for psoriasis and AD [61–63]. For psoriasis, proposed treatment targets include defined improvements in objective measures of disease severity (e.g., Psoriasis Area Severity Index [PASI], investigator global assessment [IGA], body surface area [BSA]), symptoms (e.g., pruritus) and quality of life (e.g., DLQI) [61, 62]. In comparison, defining treatable traits for AD is more challenging due to the heterogeneity of its symptoms and comorbidities, as well as their impact and importance to individual patients. Nevertheless, suggested treatment targets for AD include improvements in a combination of clinician-reported (e.g., Eczema Area and Severity Index [EASI], SCORAD, IGA, BSA) and patient-reported outcomes (e.g., Patient-Oriented Eczema Measure [POEM], Patient Global Assessment [PGA], DLQI, pruritus) [61, 63].

Dry skin is a treatable trait of psoriasis, AD, and other xerotic skin conditions; therefore, we suggest that emollient therapy is incorporated into future T2T algorithms and that treatment targets should include specific measures of xerosis cutis. Further consensus is required to establish emollient treatment targets, but they may consist of instrumental measures of skin dryness (e.g., thresholds for skin capacitance or TEWL) and xerosis-specific scoring systems (e.g., SRRC, XAS, overall dry skin score [ODS]). We believe that adopting a T2T strategy that actively optimizes emollient therapy to achieve xerosis-related treatment targets may promote adherence, limit therapeutic inertia, and improve long-term outcomes for patients with xerosis cutis and diseases associated with dry skin.

7 | Conclusions

Clinical studies of emollient therapy for managing xerosis cutis demonstrate that changes to the biophysical properties of the skin translate to improvements in clinical symptoms and patient quality of life. A wide range of study endpoints has been used to evaluate the clinical benefits of emollient therapy in patients with xerosis cutis, highlighting a need for consensus and consistent outcome measures that enable future comparative efficacy studies. Nevertheless, the current body of evidence reinforces that most emollients are safe and effective treatment options for patients with xerosis cutis. T2T strategies that incorporate emollient therapy and xerosis-specific treatment targets should be adopted in future clinical practice to improve the long-term management of xerosis cutis and diseases associated with dry skin.

Author Contributions

All authors in this supplement participated in the conceptualization of the articles to be included. For each article in this supplement, all named authors participated in the conception and design of the review, the drafting and critical review of the manuscript, and gave final approval of the version to be published.

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Conflicts of Interest

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