

A review on the role of moisturizers for atopic dermatitis

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Effective management of atopic dermatitis (AD) involves the treatment of a defective skin barrier. Patients with AD are therefore advised to use moisturizers regularly. To date, there are few comparative studies involving moisturizers in patients with AD, and no classification system exists to objectively determine which types of moisturizers are best suited to specific AD phenotypes. With this in mind, a group of experts from allergy and immunology, adult and pediatric dermatology, and pediatrics centers within Southeast Asia met to review current data and practice, and to develop recommendations regarding the use of moisturizers in patients with AD within the Asia-Pacific region. Chronicity and severity of AD, along with patient age, treatment compliance, and economic background should all be taken into account when selecting an appropriate moisturizer for AD patients. Other considerations include adjuvant properties of the product, cosmetic acceptability, and availability over the counter. Well-defined clinical phenotypes of AD could optimally benefit from specific moisturizers. It is hoped that future studies may identify such differences by means of filaggrin mutation subtypes, confocal microscopic evaluation, pH, transepidermal water loss or presence of allergy specific IgE. Recommendations to improve the regular use of moisturizers among AD patients include measures that focus on treatment compliance, patient and caregiver education, appropriate treatment goals, avoidance of sensitizing agents, and collaboration with other relevant specialists.

Keywords: Dermatitis, atopic; Compliance; Asia Pacific; Moisturizer; Classification

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INTRODUCTION

Atopic dermatitis (AD) is a chronic pruritic inflammatory disorder characterized as a defect in the skin barrier [1, 2]. This alteration in the barrier leads to increased penetration by environmental allergens and infective organisms that cause persistent inflammation in the skin. Although the barrier defect has been considered in the past as an epiphenomenon, it is now believed to play a major role in the pathophysiology of this disease [1, 2].

Since AD is chronic and relapsing, the most important treatment strategy involves treating and preventing flares, and repairing the skin barrier in the long term through adequate patient education and cooperation with the caregivers. Among the available treatment modalities, moisturizers are the basic requirement for optimal treatment of AD regardless of the severity [3]. These moisturizers hydrate the skin and repair skin barrier function [4]. Current AD management guidelines recommend moisturizer use as a key and basic step in the treatment of AD alongside avoidance of triggers and control of symptoms and inflammation [5-10].

Treatment choice of moisturizers for AD patients is largely influenced by personal preference, with few well-designed comparative studies investigating the effects of moisturizers in these patients [11]. Moreover, there is currently no clinical classification system to objectively determine which types of moisturizers are most appropriate for specific AD phenotypes. In light of these issues and the wide variation observed in treatment of AD across the Asia-Pacific region, a panel of ten experts from allergy and immunology, adult and pediatric dermatology, and pediatrics from around the Asia-Pacific region convened for a one-day meeting in June 2014 to discuss the importance of the appropriate use of moisturizers in the treatment of AD. This review highlights the topics covered in these discussions, as well as presenting recommendations reached by the panel.

THE ROLE OF MOISTURIZERS IN AD

A basic principle of treatment of AD is optimal skin care that adequately addresses the skin barrier defect. This skin barrier dysfunction manifests as an increase in transepidermal water loss (TEWL) and increased penetration of allergens and infectious agents, leading to inflammation and intense pruritus [3]. Contributing to this abnormality is a disturbed epidermal terminal differentiation leading to filaggrin deficiency and reduced natural skin lipids (Fig. 1) [2].

Moisturizers restore the ability of the intercellular lipid bilayers to absorb, retain and redistribute water [12, 13]. These agents may penetrate and contribute to the reorganization of the structure of the skin layers [14]. Moisturizers increase the hydration of the skin as measured by subjective and objective parameters [15-17].

Overall, the choice of moisturizers in practice has been dependent on the properties that physicians and their patients find most beneficial based on subjective considerations and outcomes [9, 13]. Cosmetic acceptability of the moisturizer also has to be taken into consideration if compliance and outcomes are to be improved [3, 16]. Other factors, like the availability of products over the counter and convenient packaging to carry around in adequate quantities have also been reported to be important [12].

CLASSIFICATION OF MOISTURIZERS

Moisturizers can be divided into various groups (Table 1) [18-21]. The terms moisturizers and emollients may be used alternately; however, in this review, emollients are considered to be those moisturizers made up of lipids and their compounds. These products are formulated in a variety of delivery systems including gels, oils, creams, ointments, or lotions, and have different compositions and properties to enhance efficacy [20, 21].

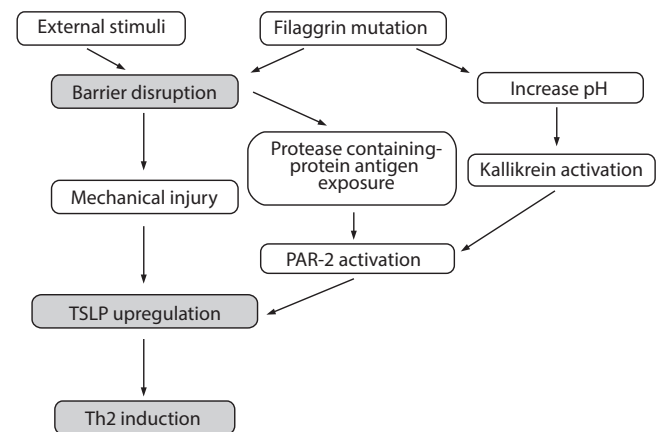


Fig. 1. Skin barrier dysfunction in patients with atopic dermatitis. TSLP, thymic stromal lymphopoietin; Th2, T helper 2 cells; PAR-2, protease-activated receptor 2. Reprinted from Kabashima K. *J Dermatol Sci* 2013;70:3-11, with permission from Elsevier [2].

Table 1. Classification of moisturizers [20, 21]

Class	Mode of action	Biological similarity	Some examples
Humectants	Attract and bind water from deeper epidermis to SC	NMF in corneocytes	Glycerin
			Alpha hydroxy acids
			Hyaluronic acid
			Sorbitol
			Urea
Occlusives	Form a hydrophobic film to retard TEWL of SC	Intercellular lipid bilayers - Ceramide - Cholesterol - Free fatty acids	Carnauba wax
			Lanolin
			Mineral oils
			Olive oil
			Petrolatum
Emollients	Smoothens skin by filling the cracks between desquamating corneocytes	Natural lipids found on skin and sebum	Silicone
			Collagen
			Colloidal oatmeal
			Elastin
			Glyceryl stearate
			Isopropyl palmitate
			Shea butter
			Stearic acid

SC, subcutaneous layer; NMF, natural moisturizing factor; TEWL, transepidermal water loss.

MOISTURIZERS AND ANTI-INFLAMMATORY MEDICATIONS

There are multiple anti-inflammatory medication options available for treating AD. Corticosteroids which are considered appropriate for most patients [18, 19]. Calcineurin inhibitors may provide alternative anti-inflammatory activity without the adverse effects associated with corticosteroids [21-23]. Recently, some of the newer anti-inflammatory agents have been added into the moisturizer formulations in order to alleviate mild-to-moderate AD [21]. These anti-inflammatory agents include glycyrrhetic acid, palmitoylethanolamine, telmesteine, *Vitis vinifera*, ceramide-dominant barrier repair lipids and flaggrin breakdown products (e.g., ceramide precursor/pseudoceramide, 5-sphingosine-derived sphingolipid, niacinamide, vitamin B3, pyrrolidone carboxylic acid, and arginine) [24]. These active agents are combined with emollients or humectants, which may provide additional barrier repair and control of xerosis [24-26].

Several such nonsteroidal, noncalcineurin inhibitor options are now available [22], of which MAS063DP was the first to be approved by the U.S. Food and Drug Administration for the relief of symptoms of AD and allergic contact dermatitis [27, 28]. MAS063DP is a nonsteroidal barrier repair cream that contains glycyrrhetic acid, *Vitis vinifera* extract and telmesteine in combination with shea butter (emollient) and hyaluronic acid (humectant). Randomized, vehicle-controlled studies have demonstrated that MAS063DP is an effective monotherapy for mild-to-moderate AD in pediatric and adult patients [26, 29].

PATIENT PHENOTYPE AND MOISTURIZERS

The severity of chronic diseases, especially AD, has an impact on the quality of life (QoL) of both the patient and the family [30]. In patients with AD, reduced QoL is commonly due to the scratching and sleep problems which are associated with a greater severity

of the disease [30]. Certain priority patient groups with similar disease morphologies have been considered to benefit from specific moisturizer types [12]. However, a clinical classification system to objectively determine which types of moisturizers are best suited for these AD phenotypes has yet to be developed.

There are several genes which contribute to skin types and mechanisms of repair implying the presence of distinct AD phenotypes; however, there is insufficient knowledge of the substrate that is necessary (i.e., moisturizer ingredients) to address the specific epidermal defect [31]. The choice of moisturizers has, therefore, been determined in clinical practice by individual preference, safety, efficacy and the absence of fragrances, additives or other sensitizing agents [18].

A panel of clinical experts from the United Kingdom has developed recommendations to address the need for guidance regarding moisturizer choice for specific types of dry skin in patients with AD [12]. For mild-to-moderate cases of AD, occlusive emollient creams were recommended depending on the thickness of barrier, variable lipid content, severity of condition and body site. For more severe AD, occlusive emollient ointment was recommended, but the panel acknowledged that this may have limited acceptability. For very severe AD, occlusive ointment with no water content can be considered. Where simple emollients are ineffective or greasier products are unacceptable, humectant containing emollients may be applied. Lastly, for pruritus, emollients containing an antipruritic agent were recommended [12]. However, the panel acknowledged that there may be difficulty in the differentiation of skin types when using this approach (e.g., “dry” versus “very dry” skin).

THE ASIA-PACIFIC PERSPECTIVE

AD is a relatively common disorder among patients in the Asia-Pacific region. In a 2-year survey in Singapore in 1989, dermatitis ranked top among the most common skin disorders amongst Chinese, Malay, and Indian patients [32]. More recently, data from an international cross-sectional survey of school children reported that the 12-month prevalence of AD in children aged 13–14 years ranged from 0.9% in China to 9% in Malaysia and Singapore [33]. The prevalence of AD in Asia-Pacific countries appears to be increasing, a fact that has been attributed to environmental and socioeconomic factors [33]. The incidence and severity of AD among Asian patients may also be affected by environmental, cultural and

dietary factors specific to the region [11]. Furthermore, evidence exists that a broader range of flaggrin gene mutations may be present in Asian populations [34, 35]. Across the Asia-Pacific region, there are marked variations in skin types, as well as large differences in socioeconomic conditions. In this region of the world, the management of AD is likely to be influenced by differences in health-care systems and access to medical care, as well as cultural diversity and variable climate. Regional survey data indicate that there is substantial variation across Asia regarding treatment practices in AD [10, 36].

Recently published consensus guidelines have focused specifically on AD in the Asia-Pacific region [10]. These guidelines recommend the regular use of moisturizer as maintenance therapy and as an adjunct to other existing therapies such as topical steroids [10]. These region-specific guidelines also noted that moisturizer use should depend not only on skin type and degree of dryness, but also the humidity of the climate.

OBSTACLES TO AD TREATMENT

Unsatisfactory treatment in AD has been attributed to misunderstanding of the disease, lack of information, inadequate self-management and nonadherence [37]. Various obstacles to patient adherence to treatment of patients with AD have been identified [38-41], and include the poor communication skills of the health-care providers; an inability to create a trusting patient-doctor relationship; a lack of adequate time to allow for patient education during the clinical visit; and the lack of effective mutual communication between patient and doctor. The lack of effective communication can lead to a failure to elicit the patient’s point of view of the disease, as well as address the patient’s concerns. A lack of discussion regarding the impact of the disease on the patient’s QoL may be perceived by the patient as a lack of empathy on the part of the doctor. Other obstacles include the noninvolvement of the patient in the treatment plan and the failure of the clinician to recognize the patient’s level of education/comprehension. The latter may thereby affect self-care, as information may not have been delivered in an age-appropriate, or culturally-sensitive manner.

Therefore, it is to be hoped that the lessons learnt from overcoming the obstacles to AD treatment in general can be more specifically applied to the use of moisturizers in particular. The development of a functional doctor-patient relationship will more fully enable guided decision-making and hence, adherence to treat-

ment, specifically the use of moisturizers.

EDUCATIONAL PROGRAMS FOR PATIENTS WITH AD

Educational programs are necessary to improve awareness in AD patients. They are effective tools for improving treatment compliance, commonly providing psychological support for patients and their caregivers [37].

Essential topics for any educational program in patients with AD include the causes or triggers of AD (particularly skin barrier dysfunction); the clinical manifestations and features of AD; treatment options and skin care focused on active disease management and a long-term maintenance plan; and environmental management.

Various comprehensive education programs are available, for example therapeutic patient education, that help patients with chronic diseases acquire or maintain the skills they need to improve their therapeutic adherence, general health and QoL [41-43].

In trials, intervention groups were shown to have positive improvement in the patient's coping behavior, sleeplessness symptoms, anxiety about corticosteroid usage, and other psychological variables [44-46]. Hence, outcomes may be improved by providing educational initiatives on top of conventional treatments for AD.

In addition, the involvement of a dermatology nurses in the care and education of patients has been shown to improve the care and control of symptoms [47].

Although originally used for nonmedical purposes, identification of specific, measurable, attainable, relevant, and time-based (SMART) goals has been increasingly used in medical practice to provide a structured guide for patients to set treatment objectives for chronic conditions [48, 49].

The objectives may be written down in the patient's personal journal. An example of this plan as applied in AD is shown in Table 2.

Patients need to be education regarding the avoidance of ingredients that have caused skin irritation such as that in cleansers and detergents, or even moisturizers [12]. It has been found that

some substances may induce a state of immunologically mediated hypersensitivity following a variable period of patient contact [50]. Thus, patients should be made aware of these irritants (e.g., neomycin, lavender, sodium lauryl sulphate, cetyl alcohol, etc.) and of allergens (e.g., peanut oil, which is an emerging cause of food allergy in Asia, fragrances, parabens).

EXPERT PANEL DISCUSSION OF CURRENT CLINICAL PRACTICE

In terms of clinical factors, the expert panel concluded that chronicity and severity of AD are primary considerations when selecting treatment for AD. The majority of the panel agreed that patient age, compliance, QoL and economic background are also crucial concerns. Adjuvant properties, cosmetic acceptability, cost, accessibility over the counter, and availability of cream or ointment formulations were considered important by most panel members when selecting a moisturizer product for their patients. Other considerations in the choice of moisturizers in practice included the patient's personal preference, which may be influenced by weather conditions, time of day and cost. Some panel members noted that they offer a selection of suitable moisturizer products and leave the final choice to individual patients. Panel members emphasized that there is a need for better scientific studies to provide an evidence base for the selection of moisturizers for individual AD patients.

The panel acknowledged that there could be well-defined clinical phenotypes of AD that would optimally benefit from specific moisturizers. However, there are currently limited data on any categorization system based on objective measures, but there may be identifiable differences based on filaggrin mutation subtypes, confocal microscopic evaluation, pH, TEWL levels, presence of allergy specific IgE in oriental versus non-oriental skin. Lastly, moisturizers prescribed to these phenotypes should be useful for both lesional and/or nonlesional skin.

Table 2. Example of SMART treatment objectives for atopic dermatitis patients using moisturizers

WHAT	The patient will be able to state the names of at least two of the topical creams used currently and why he or she is using them
WHY	To increase the patient's knowledge about his or her illness and assist with regimen adherence so that they can function independently.
WHEN	By the end of 2 weeks, the patient should be able to state the names of the medications and verbalize the purpose for using these topical creams.

SMART, specific, measurable, attainable, relevant, and time-based.

EXPERT PANEL RECOMMENDATIONS

Although the significance of moisturizer use in AD treatment is widely acknowledged, there is much variability in terms of prescription practices and patient comprehension [41]. Therefore, the panel formed recommendations for the use of moisturizer patients with AD within the Asia-Pacific region (Table 3).

A patient-centered approach

The need for moisturizers should be stressed to the patient and/or the caregiver during the clinic visit using a patient-centered approach. Time should be taken during clinic visits to discuss the objective and benefits of therapy. Instructional leaflets may be provided, along with guidance regarding the period when the patient may possibly grow out of AD (i.e., the allergy march in pediatric patients). Specific environmental triggers should be evaluated and detected to prevent future flare-ups and unnecessary dietary modification. All creams should be introduced to the patient (such as in a booklet), along with an explanation of how, and how much, should be applied. A Fingertip Unit chart can be used as guide [42].

The patient's personal preference should be considered as a means of improving their treatment compliance. Patients should be informed of the cost of creams and other treatments and less expensive creams should be selected, especially if cost is an issue. Patients should be encouraged to try a range of appropriate moisturizers. Given that heavy sedation should be avoided in school children, the appropriate use of moisturizers alone may be sufficient to treat symptoms.

A holistic approach to education

As highlighted above, moisturizing use in AD therapy can be optimized by developing SMART goals, explaining the long-term treatment plan, by being empathetic and motivating, and by being receptive to all queries from the patient and the caregiver. In order to discuss whether these goals have been met or not, a follow-up appointment should be scheduled early on during the treatment schedule.

Additional professional help

Treatment of AD should entail collaboration among specialists (e.g., dermatologists, pediatricians, immunologists, pulmonologists, ENT, ophthalmologists, allergists) to address all interrelated conditions of the patient (e.g., AD, asthma, allergic rhinitis, allergic conjunctivitis, food allergy). This ensures a holistic and thorough management of the patient's conditions.

CONCLUSIONS

AD is a chronic and relapsing condition requiring continuous care of the skin barrier defect. Management of this condition relies on effective preventive and therapeutic approaches, which need to be communicated well to the patient and the caregiver. Moisturizers are central to prevention and optimal use of the appropriate product could lead to better outcomes.

AD patients and their physicians in the Asia-Pacific region face particular challenges, and wide variation has been noted across

Table 3. Recommendations for moisturizer use in patients with AD

To improve compliance, apply a patient-centered approach to treatment.

Patient factors and preference should always be taken into consideration when choosing treatment for AD, including moisturizers.

It is important to teach patients to avoid products with irritants such as sodium lauryl sulphate, cetyl alcohol, or other strong sensitizers (e.g., neomycin preparations, lavender, etc.), as well as known allergens (e.g., peanut oil, parabens, etc.).

A holistic approach to education can provide AD patients the information to help them choose the appropriate moisturizer.

Highlight the need for consistent use of moisturizers to the patient and/or the caregiver.

Resources may include pamphlets, a finger unit chart, and written plans.

Therapeutic patient education should be carried out.

Define goals that are patient-specific, measurable, attainable, relevant, and time-based.

Additional professional help may be tapped in special circumstances.

Intervention by dermatology nurses may provide additional benefits in terms of care and control of symptoms.

If faced with recalcitrant and severe conditions or when there are co-existing conditions needing higher level of treatment (e.g., AD, asthma, allergic rhinitis, allergic conjunctivitis, and food allergy), it is important to refer to the appropriate specialty.

AD, atopic dermatitis.

Asia regarding treatment practices in AD. Together, this supports the need for advice regarding both the appropriate selection of moisturizers for AD patients and steps clinicians can take to improve the success of treatment.

Expert opinion from a panel of specialists from the Asia-Pacific region confirms that treatment choices in AD are largely influenced by treatment accessibility, cost considerations and subjective personal preference. There is evidence to support the existence of specific clinical phenotypes in AD and further research is needed to develop objective measures by which to identify these phenotypes to aid clinicians in making rationale treatment choices.

The expert panel proposed a number of recommendations that support treatment compliance, patient education and the use of well-defined treatment goals to optimize outcomes of moisturizer treatment for AD. Treatment should also be holistic and should take into consideration other existing conditions of the patient

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