Patient acceptability, efficacy, and skin biophysiology of a cream and cleanser containing lipid complex with shea butter extract versus a ceramide product for eczema

KL Hon *, YC Tsang, NH Pong, Vivian WY Lee, NM Luk, CM Chow, TF Leung

ABSTRACT

Objectives: To investigate patient acceptability, efficacy, and skin biophysiological effects of a cream/cleanser combination for childhood atopic dermatitis.

Design: Case series.

Setting: Paediatric dermatology clinic at a university teaching hospital in Hong Kong.

Patients: Consecutive paediatric patients with atopic dermatitis who were interested in trying a new moisturiser were recruited between 1 April 2013 and 31 March 2014. Swabs and cultures from the right antecubital fossa and the worst eczematous area, disease severity (SCORing Atopic Dermatitis index), skin hydration, and transepidermal water loss were obtained prior to and following 4-week usage of a cream/cleanser containing lipid complex with shea butter extract (Ezerra cream; Hoe Pharma, Petaling Jaya, Malaysia). Global or general acceptability of treatment was documented as 'very good', 'good', 'fair', or 'poor'.

Results: A total of 34 patients with atopic dermatitis were recruited; 74% reported 'very good' or 'good', whereas 26% reported 'fair' or 'poor' general acceptability of treatment of the Ezerra cream; and 76% reported 'very good' or 'good', whereas 24% reported 'fair' or 'poor' general acceptability of treatment of the Ezerra cleanser. There were no intergroup differences in pre-usage clinical parameters of age, objective SCORing Atopic Dermatitis index, pruritus, sleep loss, skin hydration, transepidermal water loss, topical corticosteroid usage, oral antihistamine usage, or general acceptability of treatment of the prior emollient. Following use of the Ezerra cream, mean pruritus score decreased from 6.7 to 6.0 (P=0.036) and mean Children's Dermatology Life Quality Index improved from 10.0 to 8.0 (P=0.021) in the 'very good'/'good' group. There were no statistically significant differences in the acceptability of wash (P=0.526) and emollients (P=0.537) with pre-trial products. When compared with the data of another ceramide-precursor moisturiser in a previous study, there was no statistical difference in efficacy and acceptability between the two products.

Conclusions: The trial cream was acceptable in three quarters of patients with atopic dermatitis. Patients who accepted the cream had less pruritus and improved quality of life than the non-accepting patients following its usage. The cream containing shea butter extract did not differ in acceptability or efficacy from a ceramide-precursor product. Patient acceptability is an important factor for treatment efficacy. There is a general lack of published clinical trials to document the efficacy and skin biophysiological effects of many of the proprietary moisturisers.

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New knowledge added by this study

- Patient acceptability is an important factor for treatment efficacy.

Implications for clinical practice or policy

- There is a general lack of published clinical trials to document the efficacy and skin biophysiological effects of many of the proprietary moisturisers.

Introduction

Eczema or atopic dermatitis (AD) is a chronically relapsing dermatosis associated with atopy, and characterised by reduced skin hydration (SH), impaired skin integrity (transepidermal water loss [TEWL]), and poor quality of life as a result

從患者接受程度、藥效和皮膚生理狀況比較使用含牛油果脂複合物和含神經酰胺的修護霜/洗面奶來治療濕疹

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目的：探討兒童濕疹患者使用修護霜/洗面奶治療的接受程度、藥效和皮膚生理狀況。

設計：病例系列回顧。

安排：香港一所大學教學醫院的小兒皮膚科門診部。

患者：2013年4月1日至2014年3月31日期間所有自願使用一種新修護霜產品的兒童濕疹患者均被列入研究範圍，並替患者評估使用含牛油果脂複合物的Ezerra洗面奶/修護霜之前和4星期後的狀況：從右側肘窩和最嚴重的濕疹位置的拭子培養、疾病重度（濕疹評分指標SCORAD）、皮膚含水量和經表皮的水分流失。患者的接受程度分為「很好」、「好」、「一般」和「不能接受」。

結果：共34名兒童濕疹患者參與本研究，其中74%表示對Ezerra修護霜的接受程度為「很好」和「好」，26%表示「一般」和「不能接受」；另外76%表示對Ezerra洗面奶的接受程度為「很好」和「好」，另24%表示「一般」和「不能接受」。參與者在使用產品前於以下幾方面均無組內差異，包括年齡、客觀SCORAD指標、瘙癢度、失眠、皮膚含水量、經表皮的水分流失、外用皮質類固醇的使用、口服抗組胺劑的使用、或對之前曾使用其他產品的接受程度。表示對Ezerra修護霜接受程度為「很好」和「好」的組別在使用後的平均瘙癢度從6.7下降至6.0（P=0.036），兒童皮膚病生活質量的平均指數則從10.0改善至8.0（P=0.021）。與過往使用其他產品的研究測試比較，參與者對洗面奶（P=0.526）和修護霜（P=0.537）的接受程度並無統計學差異。將本研究的修護霜與過往使用另一種含引發皮脂神經酰胺修護霜比較後，發現兩種產品在藥效和接受程度方面也無統計學差異。

結論：本研究中四分之三的兒童濕疹患者表示接受使用Ezerra修護霜。與使用修護霜接受程度為「一般」和「不能接受」 的組別比較，「很好」和「好」的組別有較少瘙癢，生活質量亦較佳。含有乳木果油提取成分與含有引發皮脂神經酰胺的修護霜比較，使用者在接受程度或療效方面並無差異。患者的接受性是治療功效的重要因素。發表的文獻中普遍缺乏研究潤膚霜的有效性和皮膚生理效果的臨床試驗。

of deficient ceramides in the epidermis.[1] Regular application of a moisturiser is the key step in its management. Moisturiser therapy for AD is significantly complicated by the diversity of disease manifestations and by a variety of complex immune abnormalities.[1] Filaggrin (filament-aggregating protein) and related moisturising factors have an important function in epidermal differentiation and barrier function, and null mutations within the filaggrin gene are major risk factors for developing AD.[2-6] Ceramides and related lipid products are also important components in skin barrier function.[7] Recent advances in the understanding of the pathophysiological process of AD have led to the production of new moisturisers targeted at correcting the reduced amount of ceramides and natural moisturising factors in the stratum corneum with ceramides, pseudoceramides, or natural moisturising factors.[7] Many proprietary products claim to have these ingredients, but have no or limited studies to document their clinical efficacy. Our group previously tested a number of these commercial products and found patient preference and acceptability may influence outcomes of topical treatment independent of the ingredients in these products.[8] The purposes of this study were to investigate patient acceptability of a cream/cleanser combination containing lipid complex and shea butter extract with claimed antihistaminergic properties, and evaluate its efficacy in improving the clinical and biophysiological properties of the skin in AD patients. A MEDLINE search was also performed to evaluate whether evidence of efficacy of many of the proprietary moisturisers exists.

Methods

Consecutive patients with AD who were interested in trying a new moisturiser were recruited from the paediatric dermatology clinic at a university teaching hospital in Hong Kong. Diagnosis of AD was based on the UK working group criteria.[9] In this study, SH and TEWL in the right forearm (2 cm below the antecubital flexure), and disease severity (SCORing Atopic Dermatitis [SCORAD] index) were measured. We have previously described our method of standardising measurements of SH and TEWL.[10] After acclimatisation in the consultation room with the patient sitting comfortably in a chair for 20 to 30 minutes, SH (in arbitrary units) and TEWL (in $g/m^2/h$) were then measured according to the manufacturer's instructions with the Mobile Skin Center MSC 100 equipped with a Corneometer CM 825 (Courage + Khazaka electronic GmbH, Cologne, Germany), and a Tewameter TM 210 probe (Courage + Khazaka electronic GmbH). We documented that a site 2 cm distal to the right antecubital flexure was optimal for standardisation. Oozing and infected areas were avoided by moving the probe slightly sideways.[10] The clinical severity of AD was assessed with the SCORAD index.[11,12] The SCORAD index also scores pruritus and sleep loss/disturbance on a scale of 0 to 10 (0 being not affected and 10 being most severely affected).

Patients were given a liberal supply of a trial cream containing lipid complex with shea butter extract for eczema (Ezerra [E]; Hoe Pharma, Petaling Jaya, Malaysia) and body wash (E, Hoe Pharma). The moisturiser contained STIMUTEX AS (Centerchem Inc, Norwalk [CT], US) and saccharide isomerate. The wash contained STIMUTEX AS and Amisoft (Amisoft Technologies Ltd, Brentwood, UK). The patients were instructed not to use any other moisturiser or topical treatment. Use of any medications such as topical corticosteroid or

oral antihistamine was documented. Patients were encouraged to use the test moisturiser at least twice daily on the flexures and areas with eczema. In case the emollient effect was not satisfactory, they could use their usual emollient and medications, but the frequency of such use was to be reported and they must continue with the E moisturiser. The patients were reviewed at the end of 4 weeks. Measurements of SCORAD index, Children's Dermatology Life Quality Index (CDLQI), SH, and TEWL were repeated. Patients' global or general acceptability of treatment (GAT) was recorded as 'very good', 'good', 'fair', or 'poor'.[8,13] Approval was obtained from the Clinical Research Ethics Committee of the Chinese University of Hong Kong and written informed consents were obtained from the guardian and patient.

Continuous data were expressed as mean and standard deviation. Mann-Whitney *U* test was used for intergroup comparison and Wilcoxon signed rank test for within-group comparison as a small number of patients was included. Categorical data were presented in counts. Chi squared test or Fisher's exact test where appropriate was used to compare intergroup categorical data, while McNemar's test was used to compare within-group categorical data. Fisher's exact test was used to determine the GAT of previously used proprietary products and E moisturiser and wash. All comparisons were two-tailed, and P values of <0.05 were considered to be statistically significant. The results were also compared with the data for an emollient (C) containing ceramide-precursor lipids and moisturising factors (n=24).[14]

Results

Between 1 April 2013 and 31 March 2014, 34 patients (56% boys; mean [± standard deviation] age, 12.1 ± 4.4 years) with AD were recruited and treated with applications of a moisturising cream (E). Compliance was good and patients generally managed to use the moisturiser daily. Among the patients, 74% reported 'very good' or 'good' acceptability, whereas 26% reported 'fair' or 'poor' acceptability of the moisturiser (Tables 1 and 2).

There were no intergroup differences in pre-usage clinical parameters of age, objective SCORAD index, pruritus, sleep loss, SH, TEWL, topical corticosteroid usage, oral antihistamine usage, or GAT of prior emollient (Table 2). Following use of the E cream, pruritus score and CDLQI were lower in the 'very good'/'good' group than in the 'fair'/'poor' group. Mean pruritus score decreased from 6.7 to 6.0 (P=0.036) and mean CDLQI improved from 10.0 to 8.0 (P=0.021) in the 'very good'/'good' group (Table 2).

When analysed for the association of the rating of acceptability, the acceptability of E cleanser (P=0.526) and E cream (P=0.537) was not significantly associated with their respective pre-trial products (Table 1). Patients who preferred the trial moisturiser or wash might or might not have come from the group of poor/fair acceptability of their prior emollient or wash, and vice versa. Prior products included emulsifying ointment and various other proprietary products.

When compared historically with another product containing ceramide-precursor lipids (C) that we tested in a previous report,[14] the present shea butter extract–containing cream showed similar efficacy and acceptability (Table 3). It appears that ceramide does not confer superiority in terms of acceptability and clinical efficacy.

A MEDLINE search was performed on selected common proprietary moisturisers/emollients for eczema using the following search terms in combinations: "eczema" OR "atopic dermatitis", AND "emollient" OR "moisturizer" OR "barrier" OR "barrier repair" OR "natural moisturizing factor" OR "ceramide" OR "pseudoceramide". We selected literature mainly from the past 10 years, but did not exclude commonly referenced and highly cited older articles. We included and described all randomised trials, case series, and bench studies in barrier repair therapy for eczema, with limits activated (Humans, Clinical Trial, Meta-Analysis, Randomized Controlled Trial, English, published in the past 10

TABLE 1. Global acceptability of treatment (GAT) of cream/cleanser containing lipid complex (E)

GAT score	No. (%) of patients				P value*	
	Prior emollient (n=28)	E cream (n=34)	Prior wash (n=27)	E cleanser (n=34)	Prior emollient vs E cream	Prior wash vs E cleanser
Very good	5 (17.9)	2 (5.9)	1 (3.7)	2 (5.9)	0.537	0.526
Good	13 (46.4)	23 (67.6)	16 (59.3)	24 (70.6)		
Fair	9 (32.1)	7 (20.6)	9 (33.3)	7 (20.6)		
Poor	1 (3.6)	2 (5.9)	1 (3.7)	1 (2.9)		

Abbreviation: E = Ezerra

* Fisher's exact test

TABLE 2. Acceptability and efficacy of Ezerra cream containing lipid complex

	Data*				P value			
Patient GAT	Very good/good (n=25)		Fair/poor (n=9)		-	-	-	-
Male (%)	15 (60%)		4 (44%)		-	-	0.462†	-
Age (years)	11.8 ± 4.5		13.0 ± 4.3		-	-	0.539	-
	(1) Preuse	(2) Postuse	(3) Preuse	(4) Postuse	(1) vs (2)	(3) vs (4)	(1) vs (3)	(2) vs (4)
Objective SCORAD (0-83)‡	33.4 ± 16.1	32.0 ± 15.8	29.3 ± 16.8	31.2 ± 16.5	0.397	0.859	0.419	0.878
Pruritus (0-10)§	6.7 ± 1.6	6.0 ± 2.1	5.6 ± 1.9	6.3 ± 1.9	0.036	0.200	0.151	0.591
Sleep disturbance (0-10)§	4.3 ± 3.4	4.2 ± 3.3	3.4 ± 3.6	4.8 ± 3.3	0.954	0.221	0.442	0.645
CDLQI (0-30)§	10.0 ± 5.0	8.0 ± 4.0	9.0 ± 4.6	10.3 ± 7.8	0.021	0.623	0.618	0.565
SH (au)	34.2 ± 15.9	33.1 ± 13.9	29.6 ± 13.4	30.8 ± 11.7	0.553	0.859	0.645	0.618
TEWL (g/m²/h)	11.3 ± 3.0	10.6 ± 1.7	10.4 ± 2.6	10.2 ± 1.7	0.145	0.859	0.316	0.565
Staphylococcus aureus								
Antecubital fossa	12	14	5	4	0.774	1.000	1.000†	0.703†
Worst area	14	15	5	7	1.000	0.500	1.000†	0.439†
Topical corticosteroid	20	14	6	5	0.109	1.000	0.649†	1.000†
Antihistamine	15	12	4	5	0.375	1.000	0.462†	1.000†

Abbreviations: au = arbitrary unit; CDLQI = Children's Dermatology Life Quality Index; GAT = global acceptability of treatment; SCORAD = SCORing Atopic Dermatitis index; SH = skin hydration; TEWL = transepidermal water loss

* Data are shown in No., No. (%), or mean ± standard deviation

† Fisher's exact test

‡ Eczema: <15 denotes mild, 15-40 moderate, and >40 severe

§ The higher the index, the most severely it was affected

TABLE 3. Comparative study of the cream containing lipid complex (E) with a proprietary emollient containing ceramide-precursor lipids (C)

Variable	E cream (n=34)*		C cream (n=24)*		P value	
GAT						
Very good/good	25		16		0.572	
Fair/poor	9		8		-	
Male (%)	19 (56%)		15 (63%)		0.614	
Age (years)	12.1 ± 4.4		13.8 ± 5.7		0.269	
	(1) Preuse	(2) Postuse	(3) Preuse	(4) Postuse	(1) vs (3)	(2) vs (4)
Objective SCORAD†	32.4 ± 16.1	31.8 ± 15.8	35.1 ± 17.3	30.6 ± 16.5	0.444	0.758
Pruritus	6.4 ± 1.8	6.1 ± 2.0	5.9 ± 1.9	5.5 ± 2.1	0.336	0.308
Sleep disturbance	4.1 ± 3.4	4.3 ± 3.2	4.3 ± 3.2	4.3 ± 3.0	0.756	0.949
CDLQI	9.8 ± 4.8	8.6 ± 5.2	8.2 ± 5.1	8.8 ± 6.4	0.220	0.937
SH (au)†	33.0 ± 15.2	32.5 ± 13.2	32.5 ± 13.5	37.1 ± 13.9	0.887	0.218
TEWL (g/m²/h)	11.1 ± 2.9	10.5 ± 1.7	11.6 ± 3.1	12.2 ± 3.7	0.813	0.198
Staphylococcus aureus						
Antecubital fossa	17	18	12	13	1.000	0.927
Worst area	19	22	16	18	0.408	0.404
Topical corticosteroid	26	19	13	9	0.075	0.168
Antihistamine	19	17	11	7	0.451	0.113

Abbreviations: au = arbitrary unit; C = Cetaphil Restoraderm cream (Galderma, Canada); CDLQI = Children's Dermatology Life Quality Index; E = Ezerra cream; GAT = global acceptability of treatment; SCORAD = SCORing Atopic Dermatitis index; SH = skin hydration; TEWL = transepidermal water loss

* Data are shown in No., No. (%), or mean ± standard deviation

† The C cream reduced objective SCORAD (P=0.027) and increased SH (P=0.015)

years). Editorials, letters, practice guidelines, reviews, and animal studies were excluded. In addition, the bibliographies of the retrieved articles and our own research database were also hand searched. As of 23 April 2014, 18 articles were obtained (Table 4[13,27,33-48]). The common proprietary moisturisers were included. The publications generally provided limited evidence of efficacy and biophysical effects (such as SH and TEWL), but virtually no data on patient acceptability and effects on *Staphylococcus aureus* colonisation.

Discussion

Atopic dermatitis is a chronically relapsing dermatosis characterised by pruritus, skin dryness, inflammation, secondary bacterial infection by *S aureus*, and poor quality of life.[1,15-17] The stratum corneum normally consists of fully differentiated corneocytes surrounded by natural moisturising factor and a lipid-rich matrix containing cholesterol, free fatty acids, and ceramide. In AD, metabolism of lipid and filaggrin protein is abnormal, causing a deficiency of ceramide and natural moisturising factors and impairment of epidermal barrier function that leads to increased TEWL and abnormal skin integrity.[1,4,7,18-21] Moisturisers form the first-line therapy as maintenance and therapeutic management in childhood-onset AD.[1,22,23] Hydration of the skin helps to improve dryness, reduce pruritus, and restore disturbed barrier function. Bathing without the use of moisturiser may compromise SH.[24-26]

In this study, we explored clinical efficacy and acceptability of a proprietary moisturiser (E) containing shea butter extract. The cream was acceptable as 'very good' or 'good' in about three quarters of patients with AD who tried the moisturiser, and ameliorated their pruritus and improved their quality of life.

Compliance or adherence to usage of the moisturising cream was reflected by the GAT and reported frequency of usage (times per day).[27] We did not calculate the amount of moisturising cream used because many parents/patients have discarded the tubes or failed to bring them back for weighing in previous trials. Topical steroid usage is also an important confounding factor in this study. We standardise treatment for all our patients by not changing their existing topical steroid (mometasone furoate) and other medications (ie oral antihistamine, topical immunomodulant, and Chinese medicine). In previous studies, we found that documentation of the exact amount of steroid usage (weight or frequency of usage) was difficult for similar reasons as those for moisturisers.[28] Most parents are still concerned about topical steroid usage and tend to use the minimal amount of steroid as far as possible.[29]

Alternative explanations for the modest within-group changes in pruritus and CDLQI (Table 2) include regression to the mean, detection bias, or confounding by co-treatment with topical corticosteroid or usual emollients. Our study did not demonstrate any reduction in clinical severity or *S aureus* colonisation. When compared historically with another product (C) containing ceramide-precursor lipids that we tested in a previous report,[14] although different patients were involved and the E or C products were not received by patients in the same period, the present E cream showed similar efficacy and acceptability with the use of a similar study protocol as the previous study. It appears that specific ceramide-precursor lipids do not confer superiority in terms of acceptability and clinical efficacy.

Regarding intra-group comparisons, the C cream reduced objective SCORAD index (P=0.027) and increased SH (P=0.015), whereas the E cream reduced pruritus and improved CDLQI only in the 'very good'/'good' group (Table 3). Regarding inter-group comparisons, overall there were no significant differences between the pretreatment and post-treatment parameters for the two moisturisers. We note that in the subgroup analysis, pruritus and CDLQI could be the possible contributing factors for the acceptability in the 'very good'/'good' group for the E cream.

Many proprietary emollients/moisturisers are available in the market.[7,22,30,31] Despite claims about their efficacy, little evidence has demonstrated the short- or long-term usefulness of many of these proprietary products. Ceramides, pseudoceramides, or filaggrin protein products have been studied and added to commercial moisturisers to mimic natural skin lipids and moisturising factors.[32] Anxious parents often consult their physicians for recommendation as to the choice of an ideal or perfect moisturiser for their child with AD. Physicians need to have some evidence-based understanding about these moisturisers in order to address issues raised by the parents. We performed a MEDLINE search and found that only a few of these products have published clinical data (Table 4[13,27,33-48]). The majority either do not have patient acceptability or clinical efficacy data in the scientific literature. The efficacy of ceramides and natural moisturiser factors is generally not scientifically documented. Larger-scale, properly conducted randomised controlled trials with recruitment of more study participants may validate subtle differences in clinical efficacy between different emollients. It is likely that there will be similar outcomes in efficacy if the tested emollient is compared with any other traditional emollient such as aqueous cream or Vaseline (Unilever, London, England). Commercial pharmaceutical companies are often unwilling to supply free samples of their product to compare with an inexpensive product,

TABLE 4. Results of a MEDLINE search of studies of selected proprietary moisturisers[13,27,33-48]

Moisturiser	Patient acceptability	Clinical efficacy
Aqueous cream BP	Not evaluated	Not evaluated
Aqueous cream BP	Not evaluated	Not evaluated
Cetaphil Moisturizing Cream (Galderma Pharma SA, Lausanne, Switzerland)	Not evaluated	Clinical dryness scores improved
Cetaphil Moisturizing Cream (Galderma Pharma SA, Lausanne, Switzerland)	Acceptability in three quarters of patients with atopic dermatitis	Skin dryness improved
Cetaphil Moisturizing Cream (Galderma Pharma SA, Lausanne, Switzerland)	Patient satisfaction	Not evaluated
Cetaphil Restoraderm Moisturizer (Galderma Pharma SA, Lausanne, Switzerland)	Not evaluated	Improved erythema, scaling, or dryness
Curél (Kao, Tokyo, Japan)	Not evaluated	No change in eczema severity or quality of life
Dove (Unilever, London, UK)	No data	2 Cases of contact dermatitis
EpiCeram (PuraCap Pharmaceutical, Plainfield [NJ], US)	Not evaluated	No advantages in clinical effectiveness and cost-effectiveness
Johnson's Baby Cream (Johnson and Johnson, New Brunswick [NJ], US)	No data	Johnson's baby oil for radiodermatitis not superior to Vicco Turmeric Skin Cream (Nagpur, India)
Keri cream (Novartis, Basel, Switzerland)	No data	The overall rheology of cream had little direct effect on both the moisturising efficacy and the perceived perceptual attributes for hand dermatitis
Alpha Keri (Mentholatum Australasia Pty Ltd, Scoresby, Australia)	No data	No data
Stelatopia Moisturizing Cream (Mustela, Courbevoie, France)	No data	No data
Oilatum Cream (Stiefel Laboratories Inc, Research Triangle Park [NC], US)	Not evaluated	Uncertain beneficial effects but allergic contact dermatitis from quaternium-15 in Oilatum cream
Physiogel Cream (Stiefel Laboratories Inc, Research Triangle Park [NC], US)	Not evaluated	Not evaluated
Physiogel A (Stiefel Laboratories Inc, Research Triangle Park [NC], US)	Not evaluated	Not evaluated
Sebamed Cream (Sebapharma GmbH & Co, Boppard, Germany)	Not evaluated	No significant erythema, oedema, dryness, or scaling elicited by any of the 3 test components including Sebamed Parents did not report any side-effects All 3 studied interventions used as whole body cleansers were efficacious and well-tolerated by infants
Vaseline 100% Pure Petroleum Jelly (Unilever, London, UK)	No data	No data

Abbreviations: ICAM-1 = intercellular adhesion molecule 1; SCORAD = SCORing Atopic Dermatitis index; TEWL = transepidermal water loss

even if more validated and conclusive results may be obtained by increasing the sample size in clinical trials. That is perhaps why there are so few comparative clinical studies in the medical literature.

In a wider context, AD is a complex multi-factorial atopic disease. Monotherapy targeting merely at replacement of ceramides, pseudoceramides, or filaggrin degradation products at the epidermis is often suboptimal. In particular, colonisation with *S aureus* must be adequately treated before emollient treatment can be optimised.[17]

The major hindrance to the efficacy of a moisturiser is the patient's perception as to what an ideal moisturiser should be.[8] Indeed, it is often not the product, but the patient's acceptability that determines whether it may be used consistently. Therefore, the physician caring for a patient with AD must educate and guide the parents and the patient to choose the most acceptable formulation to ensure optimal compliance.

Biophysical effects	*Staphylococcus aureus*	Reference
Increased desquamatory and inflammatory protease activity Changes in corneocyte maturity and size	Not evaluated	Mohammed et al, 2011[33]
Reduced the subcutaneous thickness of healthy skin and increased its permeability to water loss	Not evaluated	Tsang and Guy, 2010[34]
Reduction of TEWL and increased skin hydration (all P<0.01) A significantly higher level of ceramide (P<0.05) and a trend towards increased water content	Not evaluated	Simpson et al, 2013[35]
Skin hydration improved No significant improvement in SCORAD or TEWL after 2 weeks	No difference	Hon et al, 2010[27]
Skin dryness, roughness, desquamation, and sensitivity reduced	Not evaluated	Laquieze et al, 2007[36]
Increased corneometry and decreased TEWL	Not evaluated	Simpson et al, 2012[37]
Skin hydration improved No deterioration in TEWL	Not evaluated	Hon et al, 2011[13]
No data	No data	Miller et al, 2008[38]
Not evaluated	Not evaluated	Miller et al, 2011[39] Draelos, 2008[40] Madaan, 2008[41]
No data	No data	Palatty et al, 2014[42]
TEWL and skin capacitance	No data	Wang et al, 1999[43]
No data	No data	No data on MEDLINE to date
No data	No data	No data on MEDLINE to date
Not evaluated	Not evaluated	Boffa and Beck, 1996[44] Garfield, 1966[45]
Some reduction of skin erythema	Not evaluated	Yilmaz and Borchert, 2006[46]
Inhibited the development of ultraviolet light–induced erythema and thymine dimer formation in normal human skin, but did not alter the number of Ki67+ proliferating keratinocytes and the expression of p53 and ICAM-1	Not evaluated	Kemeny et al, 2007[47]
Not evaluated	Not evaluated	Dizon et al, 2010[48]
No data	No data	No data on MEDLINE to date

This open-label series confirms our previous experience in emollient research. First, patient acceptance of the strengths, types, and formulations of any novel products need to be studied, preferably in randomised controlled trials. Second, holistic efficacy studies of all clinical parameters (namely severity scores, quality-of-life indices, SH, TEWL, *S aureus* colonisation, and patient acceptance) must be included. Third, as AD is not a simple epidermal skin disease but rather a complex atopic disease, emollient alone is bound to be suboptimal in efficacy.

Conclusions

Well-designed, large-scale, randomised, placebo-controlled trials to document therapeutic effects on disease severity, skin biophysiological parameters, quality of life, and patient acceptability are needed. Patient's acceptability of a certain product is pivotal for compliance and clinical outcome. Only few of the many proprietary moisturisers for AD have

undergone clinical trials to evaluate clinical efficacy and patient acceptability.

Declaration

Drs KL Hon and TF Leung have performed research on eczema therapeutics, and written about the subject matter of filaggrin, ceramides, and emollients.

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