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Improving the quality of life of patients with inflammatory skin diseases: a multicenter evaluation of a ceramide-containing regimen in patients with atopic dermatitis, psoriasis and xerosis

Carlota Abbad-Jaime de Aragon[a*], Emilio Berna-Rico[a*], Leonor Prieto[b], Mercedes Abarquero-Cerezo[b] and Álvaro Gonzalez-Cantero[a,c]

[a]Department of Dermatology, Hospital Universitario Ramon y Cajal, Instituto Ramón y Cajal de Investigación Sanitaria, Madrid, Spain; [b]L'Oreal España S.A. Madrid, Madrid, Spain; [c]Universidad Francisco de Vitoria, Madrid, Spain

ABSTRACT

Purpose: Atopic dermatitis (AD), psoriasis and xerosis are characterized by alterations in the skin barrier leading to symptoms that severely impair patients' quality of life (QoL). This multicenter, prospective study evaluated the benefits of a 4-week ceramide-containing regimen on the symptoms and QoL of patients with AD, psoriasis, or xerosis.

Materials and methods: Clinical assessments (SCORAD, PASI, VAS), QoL and adherence to the treatment were evaluated at baseline and after 4 weeks.

Results: A total of 312 patients (109 AD, 97 psoriasis and 106 xerosis) participated in the study; 59.3% female, mean age 42.4 years, no family history of AD, psoriasis or xerosis in ~70% of patients. Significant clinical improvements after 4 weeks were reported: 61.2% reduction in SCORAD in AD; 65.5% reduction in PASI in psoriasis; and reductions in VAS for dryness, erythema and other symptoms in xerosis patients. QoL improved in all groups (67.2% AD, 64.7% psoriasis, 77.3% xerosis), with a significant proportion of patients reducing their concomitant treatments. Most patients adhered to the regimen, and no adverse reactions were reported.

Conclusions: A ceramide-containing regimen reduced the symptoms commonly associated with AD, psoriasis, and xerosis and improves patients' QoL. Limitations include the lack of control group and limiting conclusions about ceramides' contribution on effectiveness.

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Atopic dermatitis; ceramides; psoriasis; quality of life; xerosis

Introduction

Skin diseases such as atopic dermatitis (AD), psoriasis or xerosis are a common reason for dermatological consultation, both in primary care and in specialized and emergency care (1). These conditions often manifest with a significant symptom burden, negatively impacting patient quality of life (QoL). Intense itching or pain can affect sleep quality, while more visible symptoms can cause self-consciousness and potentially social isolation, worsening patients' overall psychological and health status (2).

AD occurs in approximately 3% of the worldwide population (230 million people) (3) and affects 8–9% in Spain (4, 5). Psoriasis is also highly prevalent, affecting 2% of the global population (6) and 2.3% in Spain (7). Both disease states are associated with a significant impact on patient QoL (3, 6), due to frequently related pruritus, comorbidities and social stigma. Xerosis or dry skin manifests with erythema, dry scaling or fissuring, and is a frequent sign of other skin diseases. It affects 30% to 99.1% of people older than 60 years (8). It is the main cause of pruritus among older adults, precipitating scratching, discomfort and pain, and, as such, has a profound influence on the overall QoL of those affected (8).

Topical treatments represent a cornerstone in the therapeutic management of skin diseases (9). Topical anti-inflammatory treatments, such as corticosteroids and calcineurin inhibitors, are especially recommended in AD and psoriasis for the treatment of acute flares and to reduce the risk of relapse (10–13). However, concerns exist regarding the potential impact of some of these commonly used treatments in AD and psoriasis on the skin barrier function, suggesting strategies directly aimed at restoring the skin's barrier could represent a potential adjuvant therapy for the treatment of these skin conditions (14, 15).

All three diseases cause alterations in the lipid composition of the stratum corneum (SC), the outermost layer of the skin and the body's first line of defense. Ceramides, a class of sphingolipids, play a critical role in the formation of a competent epidermal permeability barrier within the SC. They also contribute to the modulation of epidermal differentiation and proliferation, the maintenance of skin hydration and the modulation of skin immunity. Alterations in the molecular profiles and compositions of ceramides have been described in skin diseases associated with compromised permeability barrier functions (16). In AD, low levels and altered structures have been observed in several classes of ceramides; for example, EOS (contains ester-linked fatty acids and ω-OH fatty acids), EOH (contains ω-OH fatty acids and 6-hydroxy sphingosines),

CONTACT Álvaro Gonzalez-Cantero alvarogc261893@hotmail.com Department of Dermatology, Hospital Universitario Ramon y Cajal, Instituto Ramón y Cajal de Investigación Sanitaria, Madrid, Spain
*These authors contributed equally to this work.

EOP (contains ω-OH fatty acids and phytosphingosine) and NP (contains non-OH fatty acids and phytosphingosine) are reduced in lesional skin compared with the skin of healthy individuals (17, 18). This deficiency results in a defective formation of essential lipid lamellae and the lipid envelope of the corneocyte, consequently compromising the barrier function of the skin. This impaired barrier function manifests as increased skin dryness (xerosis) and a heightened sensitivity to external agents. In psoriasis, the expression profile of the ceramides differs from that of AD. AP (N-2-OH acyl-4-OH dihydrosphingosine), NP and EOS ceramide levels are decreased, while NS (contains non-OH fatty acids and sphingosines) and AS (contains α-OH fatty acids and sphingosines) are increased (16, 19). This disrupted balance leads to increased transepidermal water loss, abnormal keratinocyte differentiation, and uncontrolled proliferation resulting in the development of skin lesions (6, 16). Xerosis also manifests as an alteration of the SC, with compromised keratinocyte differentiation and dermal barrier dysfunction (8). Compared to normal skin, xerosis patients are characterized by presenting lower levels of AP, NS, NP and EOS causing abnormalities in SC lamellar architecture (19, 20).

The topical administration of ceramide-containing formulations holds significant potential for improving barrier functionality. These formulations help strengthen the structural integrity of the SC, thus improving these skin conditions (14, 15, 17, 21).

This study investigated the efficacy of a regimen containing three skin-identical ceramides (EOP, NP and AP) in improving hydration, moisture content and promotion of barrier integrity in irritated/dry skin. The treatment regimen was evaluated both alone and in combination with specific therapies (9, 15, 17, 22). Notably, the formulation incorporates MVE® technology (multi-laminar vesicular emulsion), which allows continuous, controlled, and sustained release of its moisturizing ingredients over a 24-h period.

The aim of this study, therefore, was to evaluate the benefits of this EOP, NP and AP ceramide-containing regimen in monotherapy or adjuvant therapy on the symptoms and associated QoL factors of patients with AD, psoriasis or xerosis in Spain.

Methods

This multicenter, prospective, interventional study was conducted in Spain (see Annex A).

Study participants and protocol

Adult patients ($N = 329$) with a confirmed diagnosis of mild-moderate AD (Scoring Atopic Dermatitis, SCORAD <40), chronic plaque psoriasis (Psoriasis Area and Severity Index, PASI <10), or xerosis (Visual Analogue Scale, VAS <4) were included. Particularly, patients were included if they had AD-related symptoms (dryness, erythema, roughness and/or scaling) greater than or equal to 3 points on VAS, psoriasis-related symptoms (itching, stinging/burning and/or pain) greater than or equal to 3 points on VAS, or xerosis with disease-related signs and symptoms at the time of inclusion. Exclusion criteria included patients treated with phototherapy in the last 6 months, oral corticosteroids (>7 days), immunosuppressants or biological treatments regardless of indication, presence of any skin condition that may affect the results in the opinion of the investigator, and poor language proficiency or cognitive impairment that rendered the individual unable to complete the questionnaires.

Intervention

Patients were instructed to use a commercial ceramide-containing regimen composed of a hydrating cleanser (see Annex B) once a day within their daily cleansing routine, and a ceramide-containing moisturizer (see Annex B) all over the body at least once a day for 4 weeks (also used on demand, if necessary). Importantly, no changes were made in their previously prescribed treatment. All patients received a container of ceramide-containing hydrating cleanser and moisturizer cream (enough to cover the month of treatment).

Assessments

Information was collected from each participant at baseline (Visit 1) and after 4 weeks of treatment (Visit 2). Information collected included data on age, sex, ethnicity, medical history, relevant treatments used during the study, disease/skin condition, and severity.

Clinical assessments were performed at visits 1 and 2 using the appropriate score for each condition. For patients with AD, the investigator used the SCORAD score to evaluate the extent, severity, and subjective symptoms. For psoriasis, the PASI score was used to evaluate the severity and extent of lesions. Signs and symptoms of xerosis were evaluated using seven 10-point VAS scales of dryness, erythema, roughness, desquamation, pruritus, stinging/burning and pain. The impact on patient quality of life was assessed using the Dermatology Life Quality Index-10 (DLQI-10) questionnaire (23–26).

Finally, adherence to the ceramide-containing regimen was evaluated using a Likert-type scale at the 4-week visit. Patients were also asked about tolerance and the cosmetic properties of the products used both together and individually, and about their satisfaction with the use of the whole ceramide-containing regimen.

Statistical analysis

Values are reported as mean (standard deviation [SD]) for parametric variables, median (IQR) for non-parametric variables, and n (%) for categorical variables. Normality was evaluated using Shapiro-Wilk test. Statistical significance was assessed by the Student's t-test when comparing two groups for parametric variables, while the Wilcoxon rank-sum test was applied for non-parametric variables. Pearson's χ^2 test was used for categorical variables.

Analyses were conducted using the SPSS IBM program version 25. Differences were considered statistically significant when the p-value was less than 0.05.

Ethical considerations statement

All patients included in the study were properly informed and provided signed informed consent. This study was approved by Ramón y Cajal University Hospital Ethics Committee for Research with Medicines (262-19).

Results

A total of 329 patients were recruited, of which 17 were excluded because they did not meet the selection criteria, resulting in a final sample of 312 patients (AD, $n = 109$; psoriasis, $n = 97$; xerosis, $n = 106$).

Just over half (59.3%) of the patients were female. Mean (SD) age was 42.4 (20.8) years, and approximately 70% of patients had no family history of AD, psoriasis or xerosis (Table 1).

Atopic dermatitis (AD)

A total of 109 patients with AD were included in the study. Clinical efficacy, QoL, adherence, and patient satisfaction results are detailed below.

Clinical evaluation: SCORAD

At visit 1, the mean (SD) SCORAD value for AD patients ($n = 91$) was 31.6 (12.3) points, while at visit 2, it was 12.3 (10.8), resulting in a significant improvement in the SCORAD score [mean difference; 95% confidence interval (CI)] of 61.23% (-19.4points; 17.1–21.6; $p < 0.001$) (Figure 1).

At the beginning of the study, 56% of AD patients were using a previous treatment, of which 93% reported using topical corticosteroids and 19.7% reported using antihistamines. After 4 weeks of using ceramide-containing regimen, more than 70% of the patients had stopped or reduced the use of corticosteroids (73.7%) and almost 60% had reduced or stopped the use of antihistamines (58.3%) (Figure 2).

Quality of life

DLQI questionnaire results ($n = 71$) at both visits showed a mean (SD) score of 5.3 (4.4) points at the first visit, and 1.7 (2.3) at the second visit, revealing a significant improvement in the DLQI-measured QoL of patients with AD after the use of the

Table 1. Demographic and baseline characteristics.

	AD ($n = 109$)	Psoriasis ($n = 97$)	Xerosis ($n = 106$)	Total ($n = 312$)
Gender				
Male	45 (41.3%)	50 (51.5%)	32 (30.2%)	127 (40.7%)
Female	64 (58.7%)	47 (48.5%)	74 (69.8%)	185 (59.3%)
Age (years)				
Mean (SD)	29.6 (16.4)	47.9 (16.3)	50.6 (22.3)	42.4 (20.8)
Median [IQR]	26.0 [22.0]	48.0 [24.0]	55.5 [33.8]	42.0 [33.0]
Missing	0 (0%)	1 (1.0%)	0 (0%)	1 (0.3%)
Ancestry				
Caucasian	106 (97.2%)	94 (96.9%)	104 (98.1%)	304 (97.4%)
African	2 (1.8%)	0 (0%)	0 (0%)	2 (0.6%)
Asian	0 (0%)	0 (0%)	2 (1.9%)	2 (0.6%)
Other	1 (0.9%)	3 (3.1%)	0 (0%)	4 (1.3%)
Family history of AD				
Yes	85 (78.0%)	5 (5.2%)	13 (12.3%)	103 (33.0%)
No/NS	24 (22.0%)	92 (94.8%)	93 (87.7%)	209 (67.0%)
Family history of psoriasis				
Yes	4 (3.7%)	77 (79.4%)	3 (2.8%)	84 (26.9%)
No/NS	105 (96.3%)	20 (20.6%)	103 (97.2%)	228 (73.1%)
Family history of xerosis				
Yes	13 (11.9%)	5 (5.2%)	75 (70.8%)	93 (29.8%)
No/NS	96 (88.1%)	92 (94.8%)	31 (29.2%)	219 (70.2%)

AD: atopic dermatitis; IQR: interquartile range; NS: not stated; SD: standard deviation.

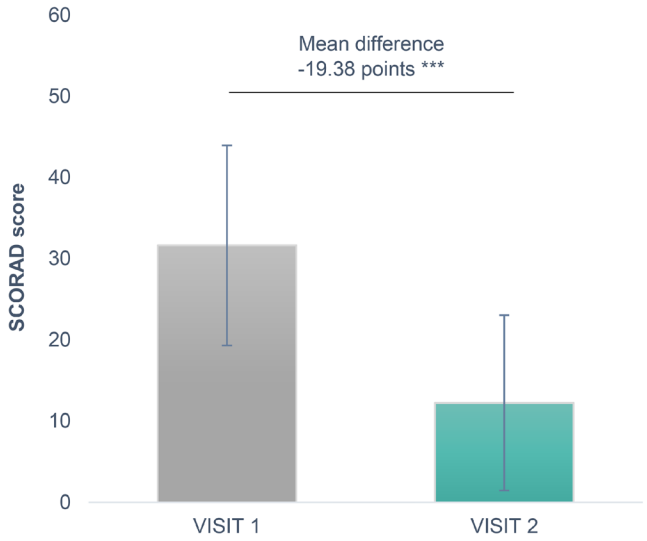

Figure 1. Mean SCORAD scores at the 1st and 2nd visit in patients with AD ($n = 91$).
***$p < 0.001$. AD: atopic dermatitis; SCORAD: Scoring AD.

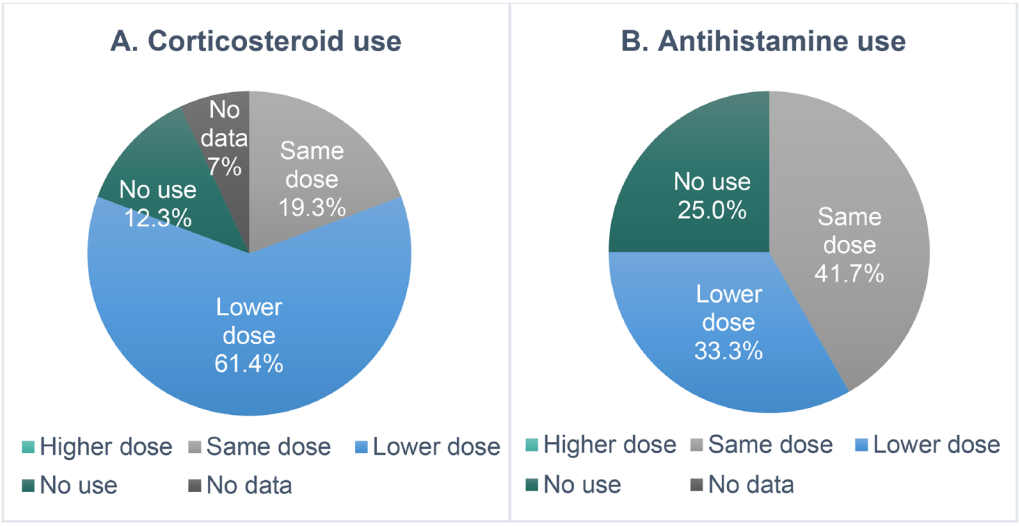

Figure 2. Use of prescribed treatments after 4 weeks of ceramide-containing regimen use in AD patients. (a) Corticosteroid use ($n = 57$), (b) Antihistamine use ($n = 12$).

ceramide-containing regimen of 67.2% (-3.6 points; 95% CI 2.8–4.4; $p < 0.001$) (Figure 3).

Adherence, cosmetic properties, and patient satisfaction

A total of 95.9% of AD patients (94/98) used the ceramide-containing regimen 3 or more times a week, with all patients using it at least once a day.

Overall, 96% of AD patients tolerated the complete ceramide-containing regimen and were satisfied or highly satisfied with the trial treatment.

The moisturizer was very well tolerated by AD patients, who gave it a mean score of 9.1 (1.1) on a scale of 1–10, highlighting features such as easy application (100%) and fast absorption (91%). The hydrating cleanser was also well tolerated, with a mean score of 8.6 (1.7) on a scale of 1–10; 93% of patients consider it a pleasant hygiene product.

No adverse reactions were observed with the use of ceramide-containing regimen in patients with available data.

Psoriasis

The same parameters were analyzed in the 97 patients with chronic plaque psoriasis as in patients with AD.

Clinical evaluation: PASI

A significant improvement of 65.5% in PASI score ($n = 71$) was observed between the results of the visit 1 (4.4 [4.7]) and those recorded after 4 weeks of using the test regimen (1.7 [2.1]), with a mean difference (95% CI) of 2.8 points (1.8–3.7; $p < 0.001$) (Figure 4).

At the beginning of the study, 56.7% of patients with psoriasis were using a previous treatment, of which 87.2% were topical corticosteroids and 14.5% antihistamines. After 4 weeks of using the ceramide-containing regimen, almost 50% of patients reduced or stopped the use of corticosteroids (48%), while 75% of those who used antihistamines discontinued their use (Figure 5).

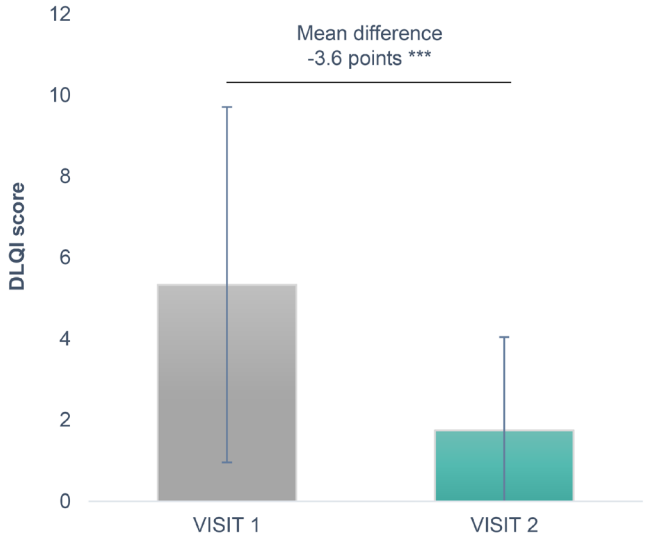

Figure 3. Mean DLQI questionnaire scores at visits 1 and 2 in AD patients ($n = 71$).
***$p < 0.001$ AD: atopic dermatitis. DLQI: Dermatology Life Quality Index.

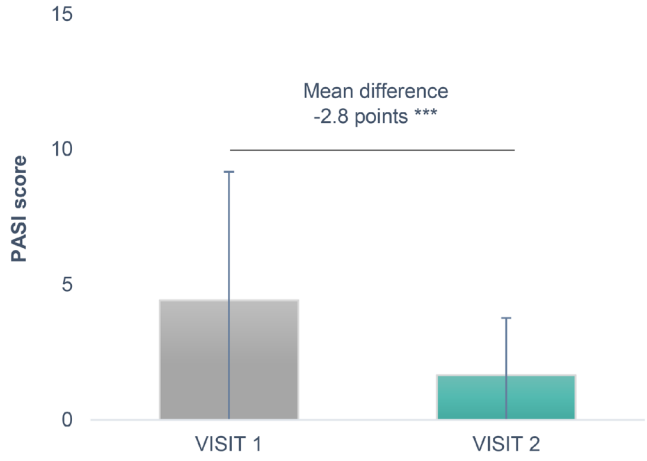

Figure 4. Mean PASI scores at the 1st and 2nd visit in patients with psoriasis ($n = 71$).
***$p < 0.001$. PASI: Psoriasis Area and Severity Index.

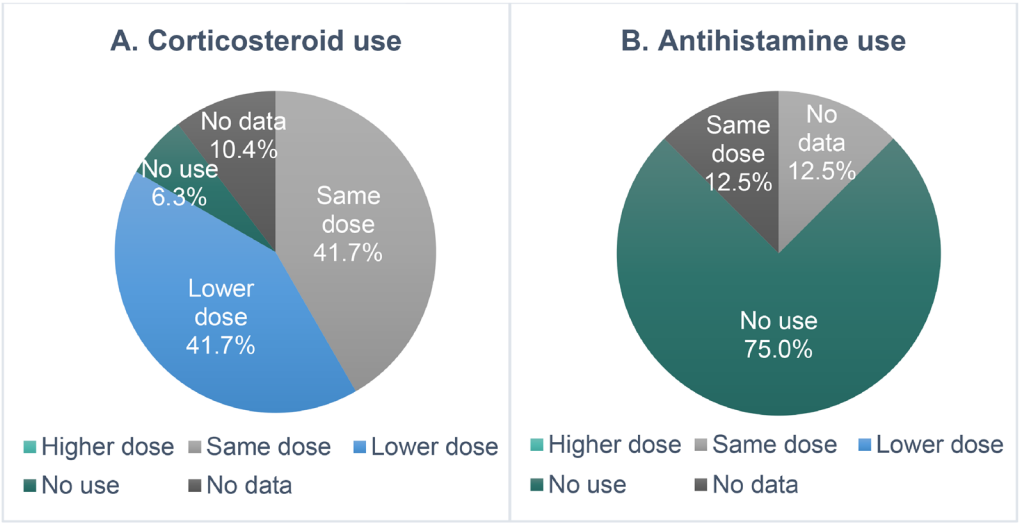

Figure 5. Use of prescribed treatments after 4 weeks of ceramide-containing regimen use in psoriasis patients. (a) Corticosteroid use ($n = 48$); (b) Antihistamine use ($n = 8$).

Quality of life

DLQI ($n = 57$) improved 64.7% in patients with psoriasis after treatment with the ceramide-containing regimen for 4 weeks. DLQI mean score was 5.3 (5.2) points at first visit, and 1.9 (2.3) at visit 2, with a mean (CI) difference between the two visits of 3.4 (2.4–4.5) ($p < 0.001$) (Figure 6).

Adherence, cosmetic properties of ceramide-containing products and patient satisfaction

Most psoriasis patients reported using the ceramide-containing regimen 3 or more times a week (90%), with the most common reported daily frequency being once a day (65.5%).

Overall, the ceramide-containing regimen was well tolerated by 96.6% of patients with psoriasis. Almost all patients were satisfied or highly satisfied with the trial treatment (96.7%).

Patients evaluated tolerance to the moisturizer and cleansing gel on a scale of 1–10. The moisturizer was well tolerated, with a mean score of 9 (1.2); the hydrating cleanser was also well tolerated, with a mean score of 8.6 (1.9). All patients (100%) found the moisturizer easy to apply and 94.4% thought it was rapidly absorbed. Regarding the cleansing gel, 95.5% of the patients described it as comfortable.

No adverse reactions were observed with the use of this regimen in patients with available data.

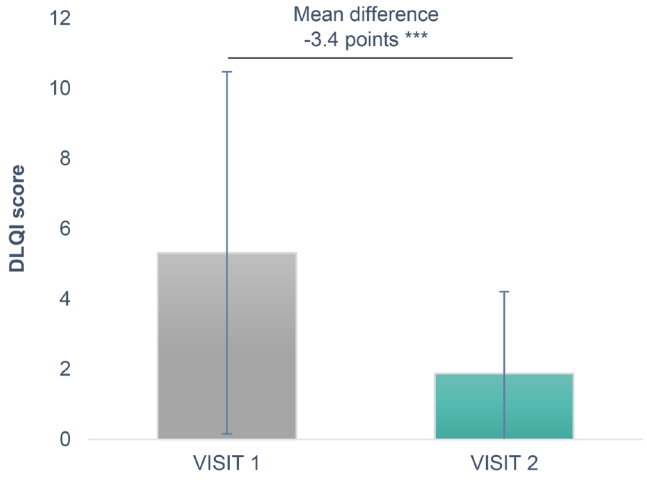

Figure 6. Mean DLQI questionnaire scores at the 1st and 2nd visits in psoriatic patients ($n = 57$). ***$p < 0.001$.

Xerosis

The impact of the ceramide-containing regimen on the signs and symptoms of patients with xerosis was evaluated.

Clinical evaluation: VAS

Dryness, erythema, roughness, desquamation, pruritus, burning, and pain were evaluated in the xerosis patient population ($n = 94$), and all symptoms showed a significant improvement ($p < 0.001$) after 4 weeks of using the ceramide-containing regimen. Mean VAS difference (95% CI) between the two visits was 63.5% (-3.9; 3.5–4.4) for dryness; 73%(-1.8; 1.4–2.2) for erythema; 69.5% (-2.7; 2.3–3.2) for roughness; 75.4% (-3.1; 2.6–3.6) for desquamation; 69.5% (-3.4; 2.1–3.9) for pruritus; 76.9% (-1.9; 1.4–2.4) for burning, and 82.2% (0.8; 0.5–1.1) for pain (Figure 7).

At the beginning of the study only 16.0% of patients with xerosis were using a previous treatment: of these, 75% were receiving topical corticosteroids and 31.2% antihistamines. After 4 weeks of using the ceramide-containing regimen, more than 80% and 60% of patients had reduced the dose or discontinued corticosteroids or antihistamines, respectively (Figure 8).

Quality of life

The QoL of xerosis patients assessed according to the DLQI questionnaire also improved after 4 weeks of using the ceramide-containing regimen. At visit 1, the mean DLQI-10 score ($n = 75$) was 3.5 (3.1) points, while at the second visit it was 0.8 (1.2), resulting in a significant improvement of 77.3% (mean difference 2.7, 95% CI 2.1–3.30; $p < 0.001$) (Figure 9).

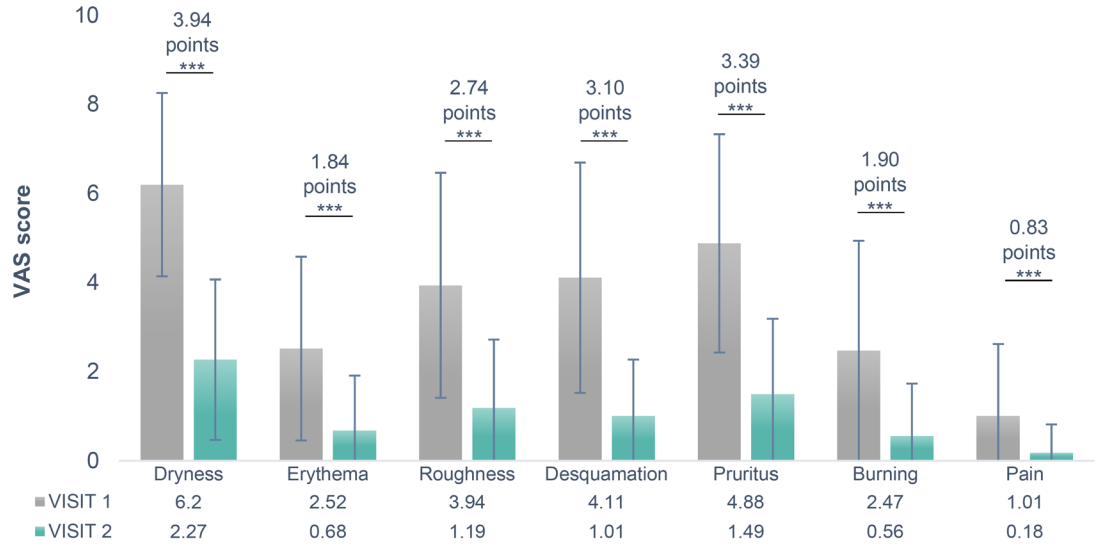

Figure 7. Results of VAS scores at first and second visit. Patients with xerosis ($n = 94$).
***$p < 0.001$. VAS: visual analogue scale

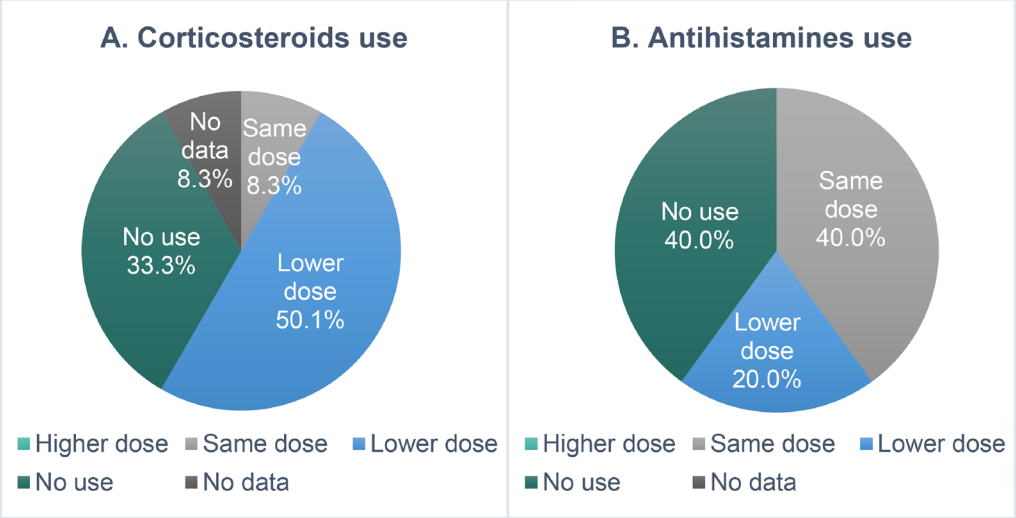

Figure 8. Use of prescribed treatments after 4 weeks of ceramide-containing regimen use in patients with xerosis. A. Corticoids use ($n = 12$), B. Antihistaminic use ($n = 5$).

Figure 9. Quality of life assessment between visit 1 and 2 in patients with xerosis.
$n = 94$. ***$p < 0.001$. DLQI: Dermatology Life Quality Index.

Adherence, cosmetic properties of ceramide-containing products and patient satisfaction

The frequency of daily and weekly use of the ceramide-containing regimen in patients with xerosis was analyzed. The most common rates of use were once a day (65%) and 3 or more times per week (89.8%).

Overall, the ceramide-containing regimen was well tolerated by 97% of xerosis patients, with almost all patients (96%) being satisfied or highly satisfied with the ceramide-containing regimen.

As regards overall tolerance, both the moisturizer (9.1/10, 1.4 SD) and the hydrating cleanser (8.5/10, 2 SD) were well tolerated. The characteristics most valued by the majority of patients were the applicability (97%) and rapid absorption (93.8%) of the moisturizer, and the pleasant sensation of the hydrating cleanser (90.9%).

No adverse reactions were observed with the use of the ceramide-containing regimen in patients with available data.

Discussion

Dermatological conditions like AD, psoriasis, or xerosis manifest in a variety of predominantly observable symptoms that impair the psychological, social, and economic well-being of affected individuals. These conditions often carry a social stigma, leading to a substantial decrease in self-esteem and contributing to social isolation. Therefore, evaluating the impact on patient QoL becomes essential when assessing the efficacy of the administered treatments (2, 27–29).

A skincare regimen, whether in monotherapy or in combination with commonly used treatments, improves the QoL of these patients. Although commonly used treatments for these conditions, such as topical corticosteroids, are effective in managing symptoms, their use is limited by potential adverse effects, such as skin atrophy and disruption of the skin barrier (30).

Ceramides constitute one of the three main lipid classes within the mammalian SC. They play a critical role in determining its biophysical properties and architecture. Notably, ceramides physically minimize transepidermal water loss (TEWL), keeping the underlying cells moisturized (31). This dysregulated composition of the skin barrier underscores the potential value of ceramide-containing skincare products in the therapeutic management of skin disorders (21, 32, 33).

The use of ceramide-containing moisturizers has been investigated in the context of inflammatory skin disorders. In a skin dryness study of 56 women treated with a ceramide-containing moisturizer with the same composition as the one used in the present study, after 4 weeks there was a 38% increase in skin water content, a 10% increase in ceramide content, resolution of the signs of dry skin and a reduction in patient-perceived discomfort (32).

Beyond enhancing skin hydration, topical ceramides improve the ceramide profile in AD patients (17). The RESTORE II study evaluated the effect of the ceramide-containing moisturizer vs a basic moisturizer in 36 women with dry skin and predisposition to AD. After 28 days and compared to the basic emollient, TEWL was reduced (-15.3 g/m^2/h) and skin barrier integrity, measured by TEWL, and lipid arrangement were improved (17). Our study confirms the positive effects of ceramide-containing skin care products in improving the symptoms associated with AD and psoriasis

(17, 32, 34–38). The use of a ceramide-containing cream and cleanser improved skin, even when used as a combined complementary regimen (36).

The ceramide-containing regimen may be useful for reducing the use of treatments including corticosteroids or antihistamines. A proportion of patients experienced a reduction or complete cessation of prior corticosteroid or antihistamine use following the ceramide-containing regimen. This potential reduction in prior medication use could decrease side effects associated with those therapies (30).

Properties such as absorption time, odor or excipients can compromise the epidermal barrier, as observed in the case of emulsifiers (9). The ceramide-containing regimen we tested was well tolerated and judged by patients as easy to apply, pleasant and quickly absorbed. No adverse effects were detected (39).

An important limitation of the study is the absence of non-ceramide controls, so we cannot establish the contribution of ceramides to efficacy or whether efficacy would be different with other moisturizers. Future comparative studies that include such controls as moisturizers versus ceramide-containing moisturizers would be of great interest.

Conclusion

For individuals with inflammatory skin conditions such as atopic dermatitis, psoriasis, or xerosis, a ceramide-containing regimen, whether used as monotherapy or in conjunction with existing treatments, helps to reduce the symptoms commonly associated with these conditions, thereby improving patients' quality of life. Furthermore, a 4-week regimen involving the application of a ceramide-containing moisturizing cream and cleanser was well tolerated, with no reported adverse events.

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Annex A. Participating Centers

Site	Principal investigator	Address
Hospital Universitario Infanta Leonor	María Ángeles Martín Diaz/Marta Valdivielso Ramos/Eva Balbín Carrero	Gran Vía del Este 80, 28031 Madrid
Hospital Universitario La Princesa	Alejandra Reolid Pérez/Alberto Fernandez Bernaldez	C/Diego De León 62, 28006 Madrid
Hospital Virgen del Valle	Cristina Pérez Hortez	Carretera De Cobisa s/n, 45004 Toledo
Hospital Universitario del Sureste	María Agustina Segurado Rodríguez/Nuria Valdeolivas Casillas/María Castellanos Gonzalez/Blanca Diaz Ley/Alicia Cabrera	Ronda del Sur 10, 28500 Arganda del Rey
Hospital Comarcal de Amposta	Yolanda Paz/Susana Bel	Carrer Jacint Verdaguer 11-13, 43700 Amposta
Hospital Plató	Alba Català/Montserrat Ferrer	Carrer de Marc Aureli 18-20, 08006 Barcelona
Hospital de Viladecans	Yolanda Fostuño/Cristina Muniesa	Avinguda de Gavà 38, 08840 Viladecans Barcelona
Hospital Vall d'Hebron	Ingrid López De Lerma	Ps. Vall d'Hebron 119-129, 08035 Barcelona
Hospital Quirón	Esther Serra Baldrich	Plz. Alfonso Comin 5 08023 Barcelona
Hospital del Mar	Gustavo Deza	Ps. Maritim de la Barceloneta 25-29, 08003 Barcelona
Hospital Germans Trías I Pujol	Anne Jaka	Crta. Canyet s/n, 08916 Badalona
Hospital Palamós	Albert Xifra	Carrer Hospital, 36, 17230 Palamós, Girona
Hospital Fundación Salut Emporda	Jaume Massana/Daniel Morgado	Rd. Rector Arolas s/n,17600 Figueres
Hospital Comarcas Inca	Enrique Casas	Vella de Llubi s/n, 07300 Inca
Hospital dos De Maig	Nuria Lamas/Ana Ravella	Dos de Maig 301, 08025 Barcelona
Hospital Galdakao	Ana Arechalde/Juan Luis Artola	Barrio Labeaga 46 A, 48960 Galdakao
Hospital Basurto	Rosa Izu	Avda. Montevideo 18, 48013 Bilbao
Hospital Urduliz	Tatiana Piqueres	Goieta kalea 32, 48610 Urduliz
Hospital Txagorritxu	Zuriñe Martínez de Lagran	José de Atxotegi s/n, 01009 Vitoria
Hospital Donostia	Lourdes Ubiria	Paseo Beguiristain 107, 20014 San Sebastián
C.S Torrelavega	Marina Lacalle	Avda. de España 8, 39300 Torrelavega
Hospital Cruces	Marta Mendieta	Plaza Cruces s/n, 48903 Barakaldo
Hospital Virgen del Rocío	Inés De Alba/Elena Baquero	Av. Manuel Siurot s/n, 41013 Sevilla
Hospital Valme	Ana Lorente	Carretera de Cádiz km 5489, 41014 Sevilla
Hospital Jerez	María Dañino	Ronda de circunvalación 11407 Jerez de la Fra. Cádiz
Hospital de Puerto Real	Celia Ceballos/Cristina Méndez	Carretera Nac IV km 665 11510 Puerto Real Cádiz
Hospital Macarena	Almudena Fernandez Orland/Ángel Marcos	Calle Dr. Fedriani 3 41009 Sevilla
Hospital Universitario de Gran Canaria Doctor Negrín	Irene Castaño González/Pedro Valeron Almaza	Plaza Barranco de la Ballena s/n, 35010 Las Palmas de Gran Canaria
Hospital Universitario Insular Gran Canaria	Dunia Esther Luján Rodríguez/Julio Orlando Rodríguez López	Avda. Marítima del Sur s/n, 35016 Las Palmas de Gran Canaria
Hospital Universitario Canarias	Nuria Pérez Robayna/Francisco José Guimera Martín-Neda	C/Ofra s/n, 38320 La Cuesta Santa Cruz
Hospital Universitario Nuestra Señora de Candelaria	Juan Ruiz León/Laura Feliciano Divasson	Carretera de Rosario 145, 38010 Santa Cruz de Tenerife
Hospital Nuestra Señora del Perpetuo Socorro	María José Rodríguez Salido	C/León y Castillo 407, 35005 Las Palmas de Gran Canaria
Hospital Vithas Santa Catalina	Azael David Freites Martínez/Rosmery Martín Moreno	C/León y Castillo 292, 35005 Las Palmas de Gran Canaria
Hospital Puerta De Hierro	Mercedes Hospital/María Antonia González De Domingo	C/Manuel de falla 1, 28222 Majadahonda
Hospital Fundación Alcorcón	Ana Pampin/Reyes Gamo	C/Budapest 1, 28922 Alcorcón
Hospital Clínico San Carlos	Lucía Campos/Sara Ibáñez	Profesor Martín lagos s/n, 28040 Madrid
Hospital La Paz	Natalia Hernández	Paseo de la Castellana 261, 28046 Madrid
Hospital 12 de Octubre	Belén Pinilla/Alba Sánchez	Avda Córdoba s/n, 28041 Madrid
Hospital Campus Del Conocimento	Francisco José Navarro Triviño	Avda del conocimiento 33, 18016 Granada
Hospital Civil	Antonio Ojeda	Plz. hospital civil s/n, 29009 Málaga
Hospital Doctor Gálvez	María Fernanda Arce	San Agustín 1, 29015 Málaga
Hospital Arnau De Vilanova	Esther Quecedo Estébanez	C/San Clemente 12, 46015 Valencia
Hospital Clínico Universitario Valencia	Luis Carlos Sáez Martín	Avda. Blasco Ibáñez 17, 46010 Valencia
Hospital De Manises	Virginia Sanz Motilva	Avda. Generalitat Valenciana 50, 46940 Manises
Hospital General Universitari d'Alacant	Mar Blanes Martínez	Avda. Pintor Baeza 12, 03010 Alicante
Hospital General Universitario De Castellón	María José Bernat García	Avda. Benicasim s/n, 12004 Castellón de La Plana
Hospital Universitari I Politecnic La Fe de Valencia	Montserrat Evole Buselli	Avda. FERNANDO ABRIL Martorell 106, 46026 Valencia
Hospital Universitario Doctor Peset	Ramón García Ruiz	Avda. Gaspar Aguilar 90, 46017 Valencia

Annex B. Hydrating Cleanser and Moisturizer Composition

Hydrating cleanser INCI: Aqua/Water, Glycerin, Cetearyl Alcohol, Phenoxyethanol, Stearyl Alcohol, Cetyl Alcohol, Peg-40 Stearate, Behentrimonium Methosulfate, Glyceryl Stearate, Polysorbate 20, Ethylhexylglycerin, Potassium Phosphate, Disodium Edta, Dipotassium Phosphate, Sodium Lauroyl Lactylate, Ceramide Np, Ceramide Ap, Phytosphingosine, Cholesterol, Sodium Hyaluronate, Xanthan Gum, Carbomer, Tocopherol, Ceramide Eop.

Ceramide-containing moisturizer INCI: Aqua/Water, Glycerin, Cetearyl Alcohol, Caprylic/Capric Triglyceride, Cetyl Alcohol, Ceteareth-20, Petrolatum, Dimethicone, Phenoxyethanol, Behentrimonium Methosulfate, Potassium Phosphate, Ethylhexylglycerin, Sodium Lauroyl Lactylate, Disodium Edta, Dipotassium Phosphate, Ceramide Np, Ceramide Ap, Phytosphingosine, Cholesterol, Xanthan Gum, Carbomer, Sodium Hyaluronate, Tocopherol, Ceramide Eop.