A Cohort Study on a Ceramide-Containing Cleanser and Moisturizer Used for Atopic Dermatitis

Charles W. Lynde, MD, FRCPC; Anneke Andriessen, PhD

Practice Points

- Skin barrier dysfunctions, such as lipid abnormalities, promote the development and severity of atopic dermatitis.
- Moisturizers and ceramide-containing moisturizers are offering concomitant therapy for atopic dermatitis patients with benefits that may reduce the need for topical steroids or shorten the period of steroid use.
- These skin care regimens may be combined with other therapies.

Atopic dermatitis (AD) is a chronically relapsing inflammatory skin disorder. In this cohort study, we evaluated the effectiveness of a twice-daily regimen of a ceramide-containing cleanser and moisturizer in men, women, and children with AD (N=151). The treatment period was 6 weeks. Participants were evaluated at baseline (day 0) and at the end of treatment (day 42) using clinical photographs, the SCORAD (SCORing of Atopic Dermatitis) index, and quality of life (QOL) assessment. Participants were randomly selected and were allocated to 1 of 2 groups: group 1 with participants 12 years and older (n=118) and group 2 with participants younger than 12 years (n=33). At day 42, SCORAD scores for group 1 showed significant improvement (t_{115}=18.33, P=.0001). Skin condition in group 2 was evaluated by the participants' guardians. At day 42, SCORAD scores for group 2 showed significant improvement (t_{27}=5.38, P=.0001). Similar effects were observed for itching, with scores that improved from very itchy to itching only when the skin was wet (t_{27}=5.38, P=.0001). No adverse events were reported during the 6-week evaluation period. The study results indicate that the ceramide-containing cleanser and moisturizer regimen substantially improved skin condition and clinical outcomes related to AD severity as well as QOL aspects.

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Atopic dermatitis (AD) is characterized by skin barrier dysfunction resulting in skin dryness, irritation, and inflammatory changes, as well as an increased risk for infection.[1-3] Atopic dermatitis often begins in childhood before 5 years of age and may persist into adulthood. For some patients, AD flares periodically and then subsides, sometimes for up to several years.[2] It is estimated that 75% of pediatric cases of AD improve by adolescence, whereas 25% continue to experience symptoms through adulthood.[1] Atopic diseases are characterized by IgE sensitization to environmental allergens. The gene-environment interactions leading to the development of AD are only partially understood.[2,3] Distinguishing between the primary events leading to AD and the secondary events resulting from AD

Dr. Lynde is from the Division of Dermatology, University of Toronto Department of Medicine, Canada, and the Lynde Centre for Dermatology, Ontario, Canada. Dr. Andriessen is from Andriessen Consultants, Malden, Netherlands, and Radboud University Nijmegen Medical Centre, Netherlands.

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Correspondence: Anneke Andriessen, PhD, Zwenkgras 25, 6581RK Malden, Netherlands (anneke.a@tiscali.nl).

is complicated by the fact that a majority of young patients rapidly outgrow the disease as they age. In early infancy, the absence of allergen-specific IgE likely is the result of an immature adaptive immune system that will gradually develop IgE-mediated sensitization to environmental allergens.[3]

The use of moisturizers has been suggested as beneficial in the treatment of patients with AD. A 4-week study comparing the effects of a high-potency topical steroid to a ceramide-containing hydrating cleanser and moisturizer cream in eczema patients showed that the ceramide-treated group had reduced SCORAD (SCORing of Atopic Dermatitis) index scores, decreased pruritus, and improved sleeping habits.[4]

The purpose of the current cohort study was to evaluate the clinical efficacy of twice-daily use of a ceramide-containing cleanser (CeraVe Hydrating Cleanser, Valeant Pharmaceuticals International, Inc) and twice-daily application of a ceramide-containing moisturizer (CeraVe Moisturizing Cream, Valeant Pharmaceuticals International, Inc) in patients with AD. Our hypothesis was that this cleanser and moisturizer regimen would demonstrate 20% or more improvement in skin condition of AD patients over a 6-week treatment period as well as improvement in aspects of quality of life (QOL).

Methods

Study Participants—The Canadian cohort study was conducted from November 2011 to June 2012 and included a 6-week study period in 151 randomly selected participants who were recruited from 30 study centers. Study participants included men, women, and children with Fitzpatrick skin types I to III and mild to moderate AD who were willing and able to give consent and comply with treatment. The participants were allocated into 2 age groups: 12 years and older (group 1: n=118) and younger than 12 years (group 2: n=33). Exclusion criteria included allergies to any ingredients in the study products; current varicella-zoster virus, herpes simplex virus, vaccinia virus, cutaneous tuberculosis, and other untreated skin infections (eg, fungal, bacterial, viral); women who were pregnant or breastfeeding; history of poor compliance with medical treatment; current use of nonsteroidal anti-inflammatory drugs for pain or skin conditions; current therapy with immunomodulators and/or bioengineered proteins (eg, antibodies, fusion proteins, recombinant cytokines), oral primrose oil, or traditional Chinese herbal treatments; and patients with facial AD or other types of dermatitis. No topical therapies were administered to the treatment areas 30 days prior to evaluation as well as during the 6-week study period. During the evaluation period, participants avoided tanning beds and sunlamps and agreed not to schedule a vacation to a sunny destination.

Assessment—All study participants (N=151) were treated with the ceramide-containing cleanser and moisturizer for 6 weeks. A clinical scale (SCORAD index[5]) was used to measure treatment outcome by comparing AD severity (ie, skin condition, QOL) at baseline (day 0) versus the end of treatment (day 42). Dermatologists may use SCORAD before and after AD treatment to assess the effectiveness of the treatment.[5] The SCORAD index is a clinical tool that was used by the investigators to score the extent of area affected by AD and the intensity of clinical findings (ie, redness, swelling, oozing/crusting, scratch marks, skin thickening, dryness). The presence of clinical signs was scored with yes or no; if yes, the intensity was scored on a 6-point scale (0=none; 5=worst). In the current study, further subjective QOL-related symptoms (ie, pruritus, sleeplessness) were scored by participants or the guardians according to a 6-point visual analog scale (0=no itch, sleeplessness, pain; 5=worst imaginable itch, sleeplessness, pain). Clinical efficacy was further assessed by a blinded investigator by comparing digital photographs taken at baseline (day 0) and at the end of treatment (day 42).

Statistical Analysis—Evaluation of the study results was performed using SPSS. A 2-tailed *t* test or analysis of variance was used to analyze skin condition at baseline (day 0) versus the end of treatment (day 42) using the SCORAD index both per individual and per group. Tests were carried out with α set at .05 and a confidence interval of 95%. Increasing the specificity of the test at a more stringent α level (eg, .01, .02) lowers the probability of type I errors but increases the type II error. It is generally accepted to use an α of .05 when analyzing study results obtained from a population size of 151 participants. The results from this study were reported with an α of .05 and a confidence interval of 95%.

Results

All 151 participants completed the study (Table 1). The age range of participants in group 1 was 12 to 88 years (mean, 38.8 years; median, 34 years). There were 33 participants younger than 12 years (group 2). At baseline, most participants had AD in more than 1 body location. As observed in many patients with AD, the skin on the flexural surfaces of the joints (ie, inner aspects of the elbows and knees) was most affected.

At baseline, skin condition scores showed that 54.3% (82/151) of participants reported having dry

Table 1.

Participant Baseline Demographics

Characteristics	Participants, n (%)		
	Group 1 (n=118)	Group 2 (n=33)	Total (N=151)
Gender			
Male	35 (29.7)	21 (63.6)	56 (31.1)
Female	83 (70.3)	12 (36.4)	95 (62.9)
Allergy			
Dairy	6 (5.1)	8 (24.2)	14 (9.3)
Hay fever/asthma	16 (13.6)	6 (18.2)	22 (14.6)
Other	0 (0)	4 (12.1)	4 (2.6)
AD location[a]			
Inner aspect of elbows	64 (54.2)	12 (36.4)	76 (50.3)
Inner aspect of knees	47 (39.8)	15 (45.5)	62 (41.1)
Neck/upper chest	4 (3.4)	9 (27.3)	13 (8.6)
Other	3 (2.5)	1 (3.0)	4 (2.6)

Abbreviation: AD, atopic dermatitis.
[a]In group 2, AD was present in multiple locations.

Table 2.

Skin Condition (SCORAD) at Baseline

Skin Condition	Participants, n (%)		
	Group 1 (n=118)	Group 2 (n=33)	Total (N=151)
Dry	77 (65.3)	5 (15.2)	82 (54.3)
Very dry	18 (15.3)	17 (51.5)	35 (23.2)
Crusting/oozing	11 (9.3)	4 (12.1)	15 (9.9)
Very crusting /oozing	51 (43.2)	1 (3.0)	52 (34.4)
Itchy	44 (37.3)	10 (30.3)	54 (35.8)
Very itchy	118 (100)	11 (33.3)	129 (85.4)

Abbreviation: SCORAD, SCORing of Atopic Dermatitis.

skin in the affected areas. Very dry skin was reported by 23.2% (35/151) of participants (Table 2).

Group 1—Over the 6-week study period, dermatitis started to clear in group 1, improving overall skin condition. Comparison of AD symptoms evaluated by dermatologists at day 0 versus day 42 showed significant reductions in severity from 100% to 26.3% of participants showing AD symptoms (t_{115}=18.33, P=.0001)(Figure 1). At baseline, crusting/oozing was reported to be present in 9.3% (11/118) of participants and very crusting/oozing in 43.2% (51/118) of participants (t_{103}=−8.51, P=.0001). At baseline, itchy skin was reported by 37.3% (44/118) of participants, and 100% (118/118) of participants reported having

very itchy skin (>30% of the day)(mean [standard deviation], 3.08 [1.31]), which had improved at day 42 to having itchy skin only when the skin was wet. The paired *t* test that was conducted showed a statistically significant improvement in AD severity in group 1 when comparing day 0 versus day 42 ($t_{103}=-8.51$, $P=.0001$). At day 42, participants reported feeling less embarrassed when their skin was exposed (eg, during sports activities) compared to baseline, which helped improve self-image, confidence, and QOL (Figure 2).

Group 2—In group 2 (n=33) the participants' skin condition was evaluated by the guardians who completed a diary. Participant skin condition at baseline is shown in Table 2. Treatment with both the cleanser and the moisturizer significantly improved the participants' skin condition scores at day 0 versus day 42 ($t_{27}=5.38$, $P=.0001$)(Figure 3). The same trend was observed for itching, which improved from very itchy skin during the day to only when the skin was wet ($t_{27}=5.38$, $P=.0001$). Irritation also significantly improved during the 42-day evaluation period ($t_{28}=2.53$, $P=.02$).

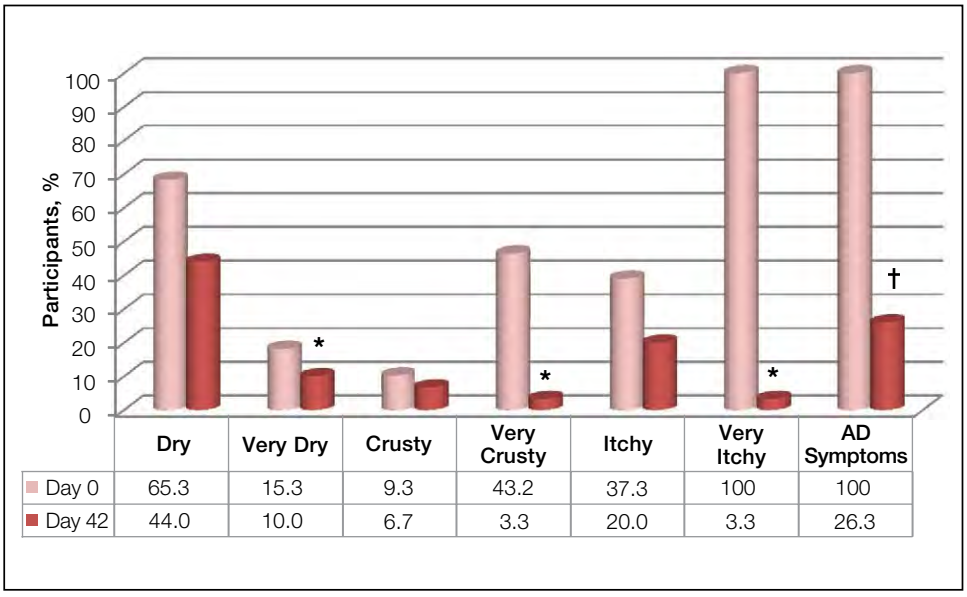

Figure 1. Reported atopic dermatitis (AD) symptoms in group 1 (n=118) of participants aged 12 years and older. Asterisk indicates $t_{103}=-8.51$, $P=.0001$; dagger, $t_{115}=18.33$, $P=.0001$.

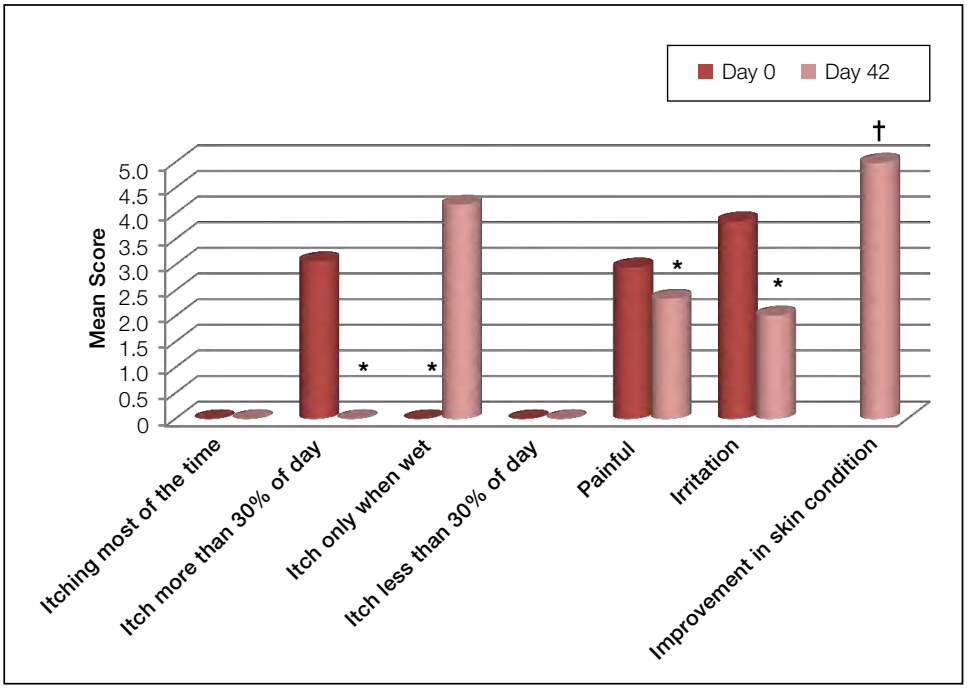

Figure 2. Participant-reported quality of life aspects at day 42 in group 1 (n=118) of participants aged 12 years and older. Scored on a 5-point scale (1=not agree; 5=strongly agree). Asterisk indicates $t_{103}=-8.51$, $P=.0001$; dagger, $t_{115}=18.33$, $P=.0001$.

This improvement also was reflected in the reported improvement of QOL aspects with improved confidence in their appearance (Figure 4).

Participant Comfort and Ease of Product Use—In both groups, the study products were rated easy and comfortable to use by all participants. Participants indicated notable improvement in QOL and were comfortable using the product, as demonstrated by good compliance reports in the diaries. No adverse events were reported during the 42-day evaluation period. Figure 5 shows typical clinical results.

Discussion

A growing body of evidence suggests that skin barrier dysfunction promotes the development and increases the severity of AD.[6] Impaired epidermal expression of claudin 1 has been reported in nonlesional skin of AD patients compared to psoriasis patients and nonatopic controls.[7,8] Defective ceramide synthesis is thought to play an important role in skin barrier dysfunction in AD.[3,6,9,10] Changes in at least 3 groups of genes encoding structural proteins, epidermal proteases, and protease inhibitors promote a

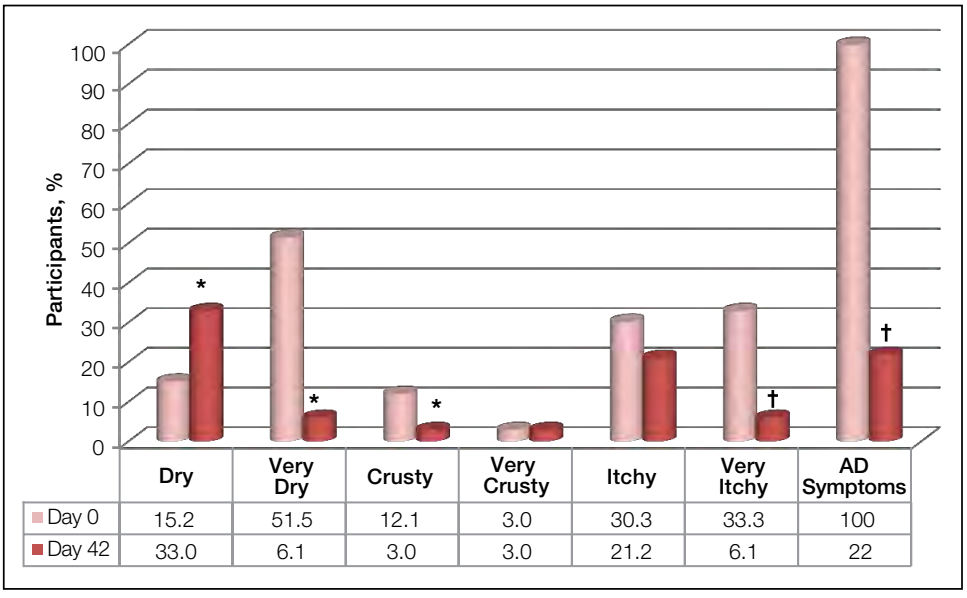

Figure 3. Reported atopic dermatitis (AD) symptoms in group 2 (n=33) of participants younger than 12 years. Asterisk indicates t_{27}=2.65, P=.01; dagger, t_{27}=5.38, P=.0001.

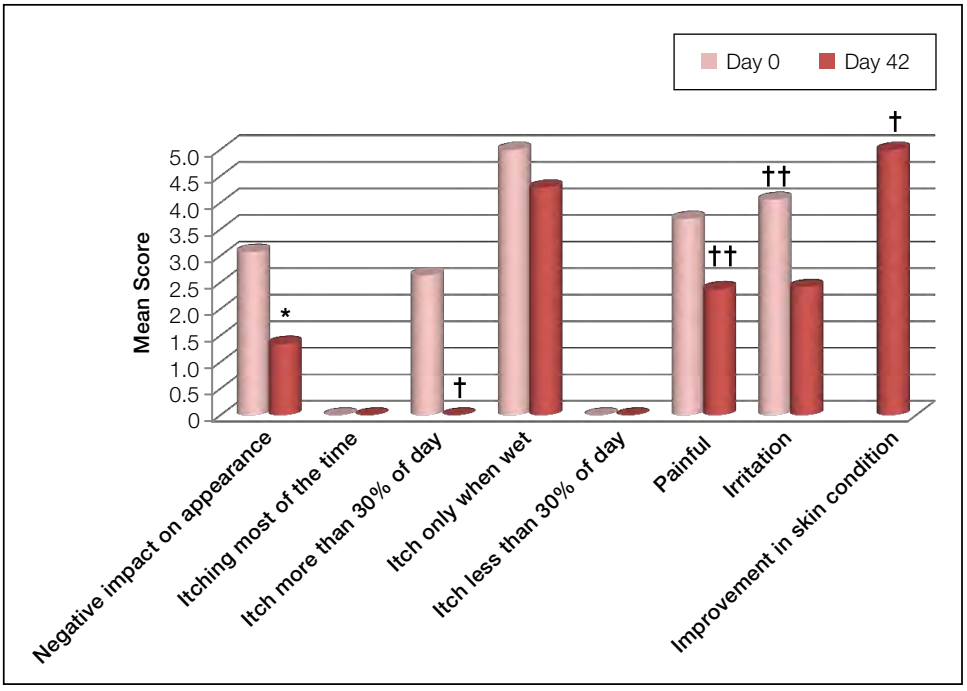

Figure 4. Guardian-reported quality of life aspects at day 42 in group 2 (n=33) of participants younger than 12 years. Scored on a 5-point scale (1=not agree; 5=strongly agree). Asterisk indicates t_{27}=2.65, P=.01; dagger, t_{27}=5.38, P=.0001; double dagger, t_{28}=2.53, P=.02.

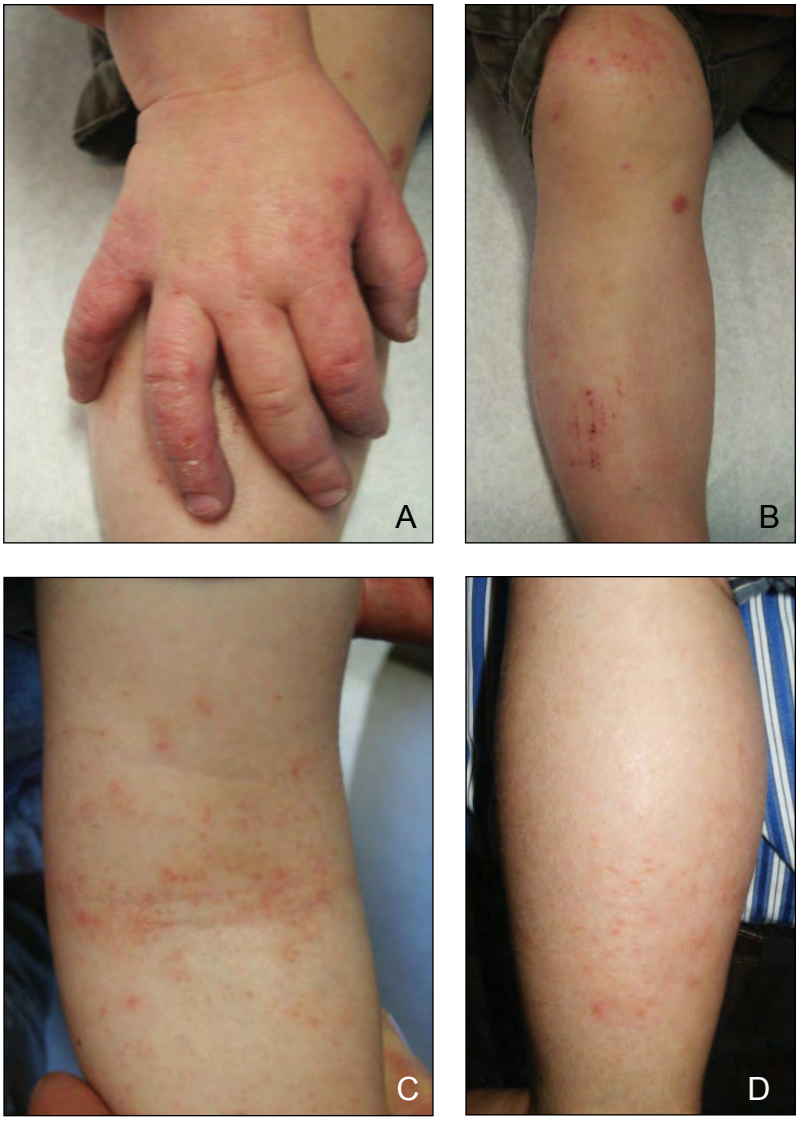

Figure 5. A 20-month-old boy with atopic dermatitis since birth on the right hand (A), right leg (B), and right antecubital fossa (C) at baseline. At day 42, improvement was noted on the right leg (D).

predisposition to a defective epidermal barrier and increase the risk for developing AD.[9,11-14] The strong association between both genetic barrier defects and environmental insults to the barrier in patients with AD suggests that epidermal barrier dysfunction is a primary event in the development of this disease.[6,9-11] There are some notable lipid abnormalities in AD, such as reductions in subcutaneous ceramides, enhanced sphingomyelin hydrolysis, and high levels of sphingomyelin deacylase expression.[6,10-14]

Topical therapies such as emollients, calcineurin inhibitors, and steroids commonly are used to treat AD.[14-17] When there is no improvement with these agents, systemic steroids are used, often in addition to gentle cleansers and moisturizers.[17] The ceramide skin care products evaluated in this study deliver 3 skin-identical ceramides—cholesterol, fatty acids, and phytosphingosine—which are essential to skin repair and skin barrier function recovery.[4,10-12] When applied to dry and/or irritated skin and inflammatory dermatoses such as AD, these products have been shown to protect, hydrate, and moisturize the skin, as well as to help rebuild epidermal lipids.[4,11,15] Ceramides, free fatty acids, and cholesterol are not likely to be incorporated into the extracellular lipids on external application, but they may aid in creating an environment for barrier repair. The study products reduce transepidermal water loss by placing a water-impervious film over the skin surface.[4,10] Our study results indicate marked improvements in SCORAD results for both groups 1 and 2. These results are in line with an earlier study.[4] Hydration of the skin using an effective moisturizer is one of the important measures involved in preserving the integrity of the

stratum corneum barrier and may reduce the need for topical steroids or shorten the period of steroid use.[4,10] Therapies directed specifically at helper T cell (T_H2) responses are being developed, mainly targeted at IgE and IL-5.[12] Therapies targeting the skin barrier either directly with ceramide-containing moisturizers or indirectly by targeting mast cells that induce scratching or the cytokines that downregulate barrier genes will most likely be beneficial in the treatment of AD patients.[12]

Because this cohort study gave descriptions of practice and did not have comparison or control groups, cause-and-effect relationships cannot be drawn.

Conclusion

The results of this cohort study indicated that the twice-daily use of a ceramide-containing cleanser and moisturizer substantially improved skin condition and clinical outcomes according to the SCORAD index as well as QOL in patients with AD. Similar results may have been obtained with a cleanser and moisturizer without ceramide; however, this comparison was not evaluated in the present study. The products were shown to be easy to use and were well tolerated in children and adults with AD.

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REFERENCES

1. Odhiambo JA, Williams HC, Clayton TO, et al. Global variations in prevalence of eczema symptoms in children from ISAAC Phase Three. *J Allergy Clin Immunol*. 2009;124:1251-1258.
2. Guttman-Yassky E, Nograles KE, Krueger JG. Contrasting pathogenesis of atopic dermatitis and psoriasis—part I: clinical and pathologic concepts [published online ahead of print March 8, 2011]. *J Allergy Clin Immunol*. 2011;127:1110-1118.
3. Bieber T. Atopic dermatitis. *N Engl J Med*. 2008;358:1483-1494.
4. Draelos ZD. The effect of ceramide-containing skin care products on eczema resolution duration. *Cutis*. 2008;81:87-91.
5. Stalder JF, Barbarot S, Wollenberg A, et al. Patient-Oriented SCORAD (PO-SCORAD): a new self-assessment scale in atopic dermatitis validated in Europe [published online ahead of print March 18, 2011]. *Allergy*. 2011;66:1114-1121.
6. Cork MJ, Danby SG, Vasilopoulos Y, et al. Epidermal barrier dysfunction in atopic dermatitis [published online ahead of print June 4, 2009]. *J Invest Dermatol*. 2009;129:1892-1908.
7. De Benedetto A, Agnihothri R, McGirt LY, et al. Atopic dermatitis: a disease caused by innate immune defects? *J Invest Dermatol*. 2009;129:14-30.
8. De Benedetto A, Rafaels NM, McGirt LY, et al. Tight junction defects in patients with atopic dermatitis [published online ahead of print December 15, 2010]. *J Allergy Clin Immunol*. 2011;127:773-786.
9. Hvid M, Vestergaard C, Kemp K, et al. IL-25 in atopic dermatitis: a possible link between inflammation and skin barrier dysfunction? [published online ahead of print September 23, 2010]. *J Invest Dermatol*. 2011;131:150-157.
10. Walling HW, Swick BL. Update on the management of chronic eczema: new approaches and emerging treatment options. *Clin Cosmet Investig Dermatol*. 2010;3:99-117.
11. Rawlings AV, Harding CR. Moisturization and skin barrier function. *Dermatol Ther*. 2004;17(suppl 1):43-48.
12. Chamlin SL, Kao J, Frieden IJ, et al. Ceramide-dominant barrier repair lipids alleviate childhood atopic dermatitis: changes in barrier function provide a sensitive indicator of disease activity. *J Am Acad Dermatol*. 2002;47:198-208.
13. Menon GK, Nórlen L. Stratum corneum ceramides and their role in skin barrier function. In: Leyden J, Rawlings A, eds. *Skin Moisturization*. New York, NY: Taylor & Francis; 2002:29-58.
14. De Paepae K, Derde MP, Roseeuw D, et al. Incorporation of ceramide 3B in dermatocosmetic emulsions: effect of the transepidermal water loss of sodium lauryl sulphate-damaged skin. *J Eur Acad Dermatol Venereol*. 2000;14:272-279.
15. Lodén M. Role of topical emollients and moisturizers in the treatment of dry skin barrier disorders. *Am J Clin Dermatol*. 2003;4:771-778.
16. Draelos ZD. Concepts in skin care maintenance. *Cutis*. 2005;76(suppl 6):19-25.
17. Lodén M. The clinical benefit of moisturizers. *J Eur Acad Dermatol Venereol*. 2005;19:672-688.