Efficacy of a Moisturizing Foam in Skin Barrier Regeneration and Itch Relief in Subjects Prone to Atopic Dermatitis

Peter A. Lio MD
Northwestern University Feinberg School of Medicine and Medical Associates of Chicago, Chicago, IL

ABSTRACT

Introduction: Atopic dermatitis (AD) is characterized by impaired epidermal barrier with increased transepidermal water loss (TEWL). Scratching further compromises skin integrity, contributing to a cycle of inflammation. The objective of the present study was to investigate a topical anti-itch foam in improving skin barrier and itch.

Material and Methods: A single center open study was performed on 26 adults previously diagnosed with AD but without active lesions. One leg was treated with a single application of an anti-itch foam. Dryness, scaling, roughness, cracking, and signs of scratching were assessed before, 6, and 24 hours after application. Skin hydration was measured at 24 hours. The same product was applied twice daily for 7.5 days to the other leg, and skin hydration and TEWL were measured at baseline and on days 2, 8, and 10. Pruritus was assessed by volunteers and by a dermatologist.

Results: A significant increase in skin moisture ($P<0.001$) was measured 6 hours after a single application. Scores of dryness, scaling, roughness ($P<0.001$) and cracking ($P=0.002$) were significantly improved up to 24 hours after a single application. After a 7.5-day repeated application period, the anti-itch foam significantly reduced TEWL ($P<0.001$) compared to baseline. Skin hydration significantly improved ($P<0.001$) in the same time period. 48 hours after the last application, these improvements remained significant ($P<0.001$).

Conclusions: The anti-itch foam improved the skin barrier. It provided immediate relief of clinical signs of AD including pruritus. Moreover, it delivered a long-lasting moisturizing effect, comforting the skin, and improving overall skin condition.

J Drugs Dermatol. 2016;15(suppl 11):s77-80.

INTRODUCTION

Skin prone to atopic dermatitis (AD) is commonly characterized by an impaired epidermal barrier that results in increased transepidermal water loss (TEWL) and leaves the skin rough, dry, and itchy.[1] Subsequent scratching behavior further compromises the integrity of the skin, contributing to a cycle of inflammation.[2] This "itch-scratch cycle" fuels the disease and likely leads to increased penetration of irritants, allergens, and infectious agents that cause persistent inflammation in the skin and may actually lead to the development of other immunologic alterations.[2,3] Although the barrier defect has been considered a secondary phenomenon in some models,[4] the most modern conception of the disease suggests that skin barrier function is a fundamental component of AD that must be addressed.[5]

It is well established that appropriate moisturizers can help restore barrier function and alleviate symptoms of AD.[6,7]Further, topical anti-itch preparations provide direct relief of pruritus but also likely work to abate the itch-scratch cycle.[8]

The anti-itch foam preparation used in the study was formulated with glycerol, a powerful humectant which also has anti-irritant, barrier-restoring, and even antimicrobial effects, all of which make it an excellent choice in patients with AD.[9] Additionally, the foam contains a proprietary synthetic avenanthramide based on the active ingredient in colloidal oatmeal that possesses anti-irritant, anti-itch and antihistaminic properties.[10,11]Remarkably, this component has been shown to actually reduce redness and itch in irritated skin as a monotherapy.[12]

The objective of the present study was to investigate a topical anti-itch foam in skin barrier regeneration and itch alleviation.

MATERIALS AND METHODS

A single center open clinical study was performed. A total of 42 subjects were screened, and 26 subjects were enrolled (average age, 30.4; range, 21.6-44.7 years) with dry and pruritic skin who had previously been diagnosed with AD, but were without active lesions at enrollment (Table 1).

One leg was treated with a single application of an anti-itch foam. Clinical scores for dryness, scaling, roughness, cracking, and clinical signs of scratching were assessed by a dermatologist before, 6, and 24 hours after the application. In addition, skin hydration was measured at 24 hours.

The same product was applied twice daily for 7.5 days to the other leg. Skin hydration and TEWL were measured at baseline and on days 2, 8, and 10 by means of corneometry and tewametry. Volunteers assessed pruritus intensity during the study using

TABLE 1.

Demographic Data and Baseline Characteristics

		(N=26)
Age (years)	N	26
	Mean ± SD	30.4 ± 6.0
	(Min,Max)	(21.6,44.7)
BMI ($kg.m^{-2}$)	N	26
	Mean ± SD	24.4 ± 4.0
	(Min,Max)	(17.1,32.8)
Gender	N	26
	Female	20 (76.9%)
	Male	6 (23.1%)
Skin phototype	N	26
	II	1 (3.8%)
	III	22 (84.6%)
	IV	1 (3.8%)
	V	1 (3.8%)
	VI	1 (3.8%)

a visual analog scale. Pruritus severity was also assessed by a dermatologist based on evaluation of the skin and interview of the volunteers.

The intra-individual difference between before and after application was analyzed using either a Wilcoxon Signed Rank test or a paired Student t-test depending on the distribution of the population, testing the hypothesis of equality. The *P*-value was to be less than 0.05 to declare significance.

RESULTS

At day 1 (baseline), 100% of patients reported itching and scratching and 88% of patients reported redness. At day 8, 50% of patients (13/26) did not have any itching sensations, 58% of patients (15/26) reported not needing to scratch, and 88% of patients (23/26) did not have redness due to scratching.

Clinical scores of dryness, scaling, roughness ($P<0.001$), and cracking ($P=0.002$) were significantly improved up to 24 hours after a single application (Figure 1).

Corneometry after a single application of product showed that the skin hydration was significantly increased at 6 hours after application and returned to baseline by 24 hours after application (Figure 2).

For the 7.5-day repeated application period, the anti-itch foam significantly reduced TEWL ($P<0.001$) compared to baseline on and beyond day 2. Moreover, skin hydration significantly improved ($P<0.001$) in the same time period (Table 2). Forty-eight hours after the last application, these improvements still remained significant ($P<0.001$).

These results were further supported by volunteer self-evaluations: the itch intensity and urge to scratch was clearly diminished after just one week of product application. This was confirmed by the dermatologist via the pruritus severity assessments (Table 3).

Overall, 7 subjects experienced a total of 8 adverse events of mild to moderate severity. These included rhinopharyngitis, a common cold, headache, and stomach ache and were determined not to be related to the study product. No serious adverse events occurred during the study.

DISCUSSION

In the past decade, there has been an intense focus on the primacy of the skin barrier in the pathophysiology of AD, particularly with the description of mutations in the *FLG* gene encoding filaggrin, a key skin protein in barrier function.[13, 14] However, even in the absence of mutations in *FLG*, the presence of inflammatory mediators actually downregulates filaggrin production, resulting in a functionally impaired skin barrier.[15] At the same time there has been increased attention devoted to itch, the cardinal symptom of AD, but with noted unmet needs for this troublesome problem.[16]

FIGURE 1. Moisturizing foam demonstrates immediate effect on skin prone to atopic dermatitis following a single application.

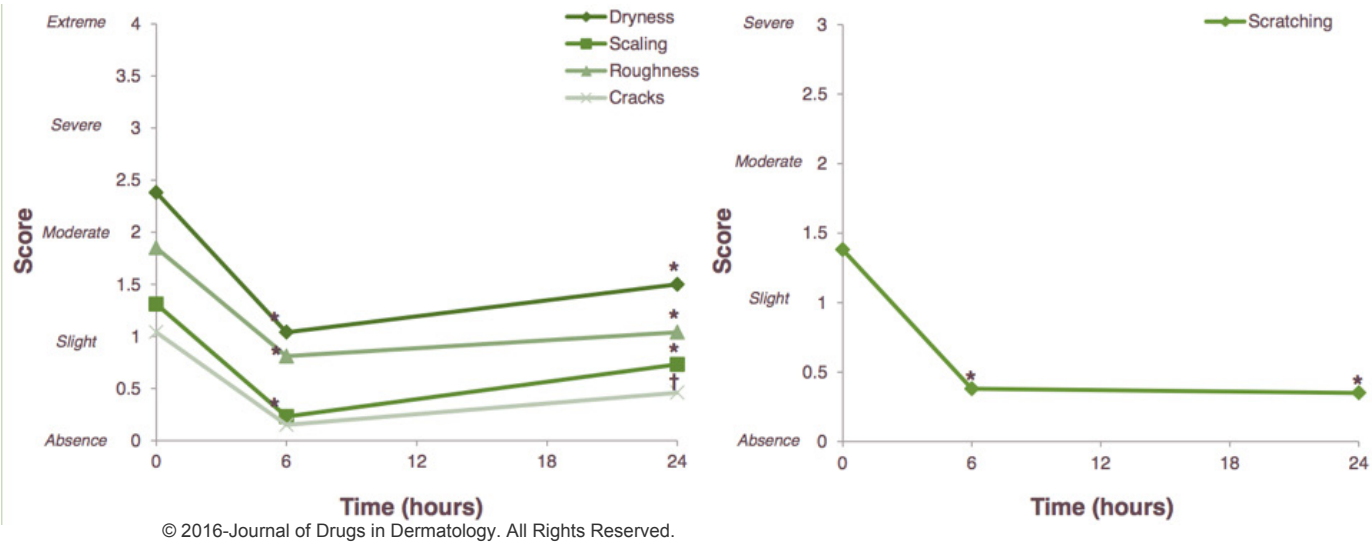
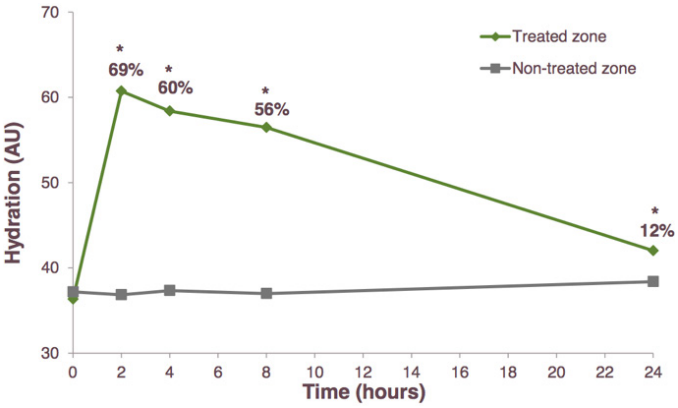


FIGURE 2. Moisturizing foam has an immediate effect on skin hydration after a single application on subjects with AD (n=20).



This study was conducted to assess the effect on skin moisturizing, skin barrier regeneration, and itch relief of an anti-itch foam. The anti-itch foam was demonstrated to strengthen the skin barrier, improving TEWL and corneometry significantly after one application and throughout the longer twice-daily application period. It provided an immediate relief of clinical signs of AD, including pruritus as assessed by both the subjects and the investigators. Moreover, it delivered a long-lasting moisturizing effect, comforting of the skin, and improvement of overall skin condition.

Associated itch was rapidly relieved and need to scratch significantly decreased within the first hours of the foam use. This anti-itch effect persisted for 48 hours after the last application. The early and durable anti-itch effect, the softening effect on the skin, and the cosmetic properties of the foam (easy to apply, rapidly absorbed) resulted in a 100% compliance.

In this study, it was shown that a twice-daily application of the foam induced a skin moisturizing effect detected from the first 24 hours. Following a 1-week treatment period, the skin remained moisturized 48 hours after ceasing product application. The moisturizing effect as assessed by corneometry was long-lasting as it was still observed after 6 hours following a single application but faded after 24 hours, justifying an at least twice-daily regimen. Clinical scores (dryness, scaling, roughness, cracks, and scratch signs) assessed by investigators however were all significantly improved at 24 hours after a single application.

Similarly, the regeneration of the skin barrier started as soon as 24 hours following the first application and this improvement was still significant 48 hours after the last product application.

In conclusion, in patients with dry, sensitive, and itchy skin prone to AD, the anti-itch foam applied twice daily for 7 days proved to have a very good moisturizing effect and to be able to repair a deficient skin barrier. Associated itch was rapidly and durably relieved and need to scratch significantly decreased as well. These suggest that the anti-itch foam product may play a role in managing symptoms of AD.

TABLE 2.

Biophysical Measurements Mean Values Over Time

	Time	N	Mean ± SD	Product effect[1]	Remanence[2] (48h)
TEWL	Day 1 (T0)	26	15.58 ± 7.63	-	
	Day 2	26	11.58 ± 5.54	**p<0.001**	
	Day 8	26	9.07 ± 5.50	**p<0.001**	
	Day 10	26	8.85 ± 3.38	**p<0.001**	p=0.949 (ns)
Corneometry	Day 1 (T0)	26	25.11 ± 8.94	-	
	Day 2	26	28.42 ± 7.71	**p=0.007**	
	Day 8	26	35.35 ± 10.53	**p<0.001**	
	Day 10	26	30.70 ± 9.43	**p<0.001**	**p<0.001**
pH	Day 1 (T0)	26	4.85 ± 0.47	-	
	Day 8	26	5.26 ± 0.65	**p=0.011**	

[1]Compared to baseline (TO)
[2]Compared to day 8

TABLE 3.

Mean Values of Pruritus Over Time

	Time	N	Mean ± SD	Product effect[1]	Remanence[2] (48h)
Intensity (assessed by the subject)	Day 1 (T0)	26	60.50 ± 15.71	-	
	Day 2	26	34.81 ± 23.65	**p<0.001**	
	Day 8	26	18.54 ± 16.82	**p<0.001**	
	Day 10	26	20.50 ± 21.75	**p<0.001**	p=0.562 (ns)
Severity (assessed by the investigator)	Day 1 (T0)	26	3.31 ± 0.84	-	
	Day 2	26	0.96 ± 1.28	**p<0.001**	
	Day 8	26	0.58 ± 0.81	**p<0.001**	
	Day 10	26	0.50 ± 0.86	**p<0.001**	p=0.835 (ns)

[1]Compared to baseline (TO)
[2]Compared to day 8

DISCLOSURES

Dr. Lio has served as a consultant/advisor and speaker for Valeant, Regeneron/Sanofi and Pierre Fabre, a consultant/advisor for Anacor, AO Biome, Exeltis, Galderma, Johnson & Johnson, Theraplex, and Mission, and has received an honrorium for his work on this supplement sponsored by Galderma.

REFERENCES

1. Giam YC, Hebert AA, Dizon MV, Van Bever H, Tiongco-Recto M, Kim KH, Soebono H, Munasir Z, Diana IA, Luk DC. A review on the role of moisturizers for atopic dermatitis. *Asia Pac Allergy*. 2016; 6:120-128.
2. Kabashima K. New concept of the pathogenesis of atopic dermatitis: interplay among the barrier, allergy, and pruritus as a trinity. *J Dermatol Sci*. 2013; 70:3-11.
3. Vijayanand P, Seumois G, Simpson LJ, Abdul-Wajid S, Baumjohann D, Panduro M, Huang X, Interlandi J, Djuretic IM, Brown DR, Sharpe AH, Rao A, Ansel KM. Interleukin-4 production by follicular helper T cells requires the conserved Il4 enhancer hypersensitivity site V. *Immunity* 2012; 36:175–187.
4. Zheng T, Jinho Y, Oh MH, et al. The atopic march: progression from atopic dermatitis to allergic rhinitis and asthma. *Allergy Asthma Immunol Res*. 2011; 3:67-73.
5. Zaniboni MC, Samorano LP, Orfali RL, Aoki V. Skin barrier in atopic dermatitis: beyond filaggrin. *An Bras Dermatol*. 2016; 91:472-478.
6. Cork MJ, Britton J, Butler L, Young S, Murphy R, Keohane SG. Comparison of parent knowledge, therapy utilization and severity of atopic eczema before and after explanation and demonstration of topical therapies by a specialist dermatology nurse. *Br J Dermatol*. 2003;149:582-589.
7. Lindh JD, Bradley M. Clinical Effectiveness of Moisturizers in Atopic Dermatitis and Related Disorders: A Systematic Review. *Am J Clin Dermatol*. 2015; 16:341-359.
8. Metz M, Staubach P. Itch Management: Topical Agents. *Curr Probl Dermatol*. 2016; 50:40-45.

9. Fluhr JW, Darlenski R, Surber C. Glycerol and the skin: holistic approach to its origin and functions. *Br J Dermatol*. 2008;159:23-34.
10. Fowler JF, Nebus J, Wallo W, Eichenfield LF. Colloidal oatmeal formulations as adjunct treatments in atopic dermatitis. *J Drugs Dermatol*. 2012; 11:804-807.
11. Sur R, Nigam A, Grote D, Liebel F, Southall MD. Avenanthramides, polyphenols from oats, exhibit anti-inflammatory and anti-itch activity. *Arch Dermatol Res*. 2008; 300:569-574.
12. Schmaus G et al. Dihydroavenanthramide D for anti-irritant and anti-itch. *Cosmetics and Toiletries*. 2007; 122:55-66.
13. Irvine AD, McLean WH. Breaking the (un)sound barrier: filaggrin is a major gene for atopic dermatitis. *J Invest Dermatol*. 2006; 126:1200-1202.
14. Palmer CN, Irvine AD, Terron-Kwiatkowski A, et al. Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis. *Nature genetics*. 2006; 38:441-446.
15. Howell MD, Kim BE, Gao P, Grant AV, Boguniewicz M, Debenedetto A, Schneider L, Beck LA, Barnes KC, Leung DY. Cytokine modulation of atopic dermatitis filaggrin skin expression. *J Allergy Clin Immunol*. 2007; 120:150-155.
16. Kamata Y, Tominaga M, Takamori K. Itch in Atopic Dermatitis Management. *Curr Probl Dermatol*. 2016; 50:86-93.

AUTHOR CORRESPONDENCE

Peter A. Lio MD
E-mail:..... p-lio@northwestern.edu