A Single-Center, Double-blind Pilot Study of the Effects of a Novel Barrier Repair Product in Patients With Atopic Dermatitis: Results of a Case Report

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Atopic dermatitis is a common disorder that affects many individuals and has a variety of treatment options available for patients. Barrier skin protection has become a recognized modality to be part of the armamentarium for clinicians treating this condition. This article describes clinical study results for a novel barrier repair formulation. The patients in this trial displayed improvement in the signs and symptoms associated with atopic dermatitis over traditional moisturization, including improvement in transepidermal water loss. The novel barrier repair product presented in this article may be useful for patients suffering from atopic dermatitis.

Atopic dermatitis is a common, chronic, noncontagious skin condition that causes irritation of the epidermis. Atopic dermatitis is a pruritic, eczematous skin condition that may follow many patients from infancy and early childhood into puberty, as well as adulthood in some afflicted with this condition.[1]

The exact etiology of atopic dermatitis is still not fully understood. There is an immunologic basis to atopic dermatitis, with many patients suffering from atopic dermatitis having elevated serum levels of serum immunoglobulin E (IgE), although no true relationship exists between IgE levels and disease severity. Genetics also plays a role in atopic dermatitis, with over one half of affected individuals having a history of atopy, which is a family history of atopic dermatitis, allergic rhinitis, asthma, or all 3. Association with defects in genes associated with filaggrin, an epidermal protein critical for skin barrier function, has been recently described.[2]

Prevalence rates for atopic dermatitis in children are reported to be between 7% to 17%, with an even smaller percentage continuing into adulthood or displaying the first outbreak in adulthood. Clinical studies have demonstrated that approximately 60% of patients with atopic dermatitis have their first outbreak by age one, and by age 5, 90% of patients display their first outbreak.[3]

In 1997, Leung et al[4] published criteria for the diagnosis of atopic dermatitis. The criteria are divided into major and minor, with 3 or more needed in each category for a true diagnosis of atopic dermatitis to be made. From the major category, patients must exhibit 3 or more of the following: pruritus; typical morphology and distribution;

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flexural lichenification in adults; facial and extensor involvement in infants and children; chronic dermatitis or chronically relapsing dermatitis; and a personal history of atopy (eg, asthma, allergic rhinitis, atopic dermatitis). Minor criteria of 3 or more are also required and include cataracts; cheilitis; recurring conjunctivitis; eczema with perifollicular accentuation; facial pallor or erythema; food intolerance; nonallergic hand dermatitis; ichthyosis; elevated IgE; immediate (type I) skin test reactivity; cutaneous infections; Dennie-Morgan infraorbital folds; pruritus when sweating; keratoconus; keratosis pilaris; nipple dermatitis; orbital darkening; palmar hyperlinearity; pityriasis alba; white dermographism; wool intolerance; and xerosis.

A variety of treatment options exists for patients with atopic dermatitis.[5] The treatments may be divided into several classes, including general skin care; topical corticosteroids; antihistamines; systemic corticosteroids; topical calcineurin inhibitors; and oral immunosuppressive agents. There are a variety of agents available in each of these classes, which have been shown to be useful in patients with atopic dermatitis. Dermatologists have preached for many years the importance of skin care in patients with atopic dermatitis, as evidence has continued to surface that the barrier properties of the skin are altered and affected, leading to possible exacerbations in the disease process.

Many compounds have recently been developed to address the barrier properties of the skin. A novel compound has recently been introduced, and this study was designed to evaluate this new compound compared to routinely prescribed moisturizers, which remain the most commonly used products with barrier properties at this time.

A novel barrier repair product was developed and contains 4 functional ingredients blended into a moisturizing lotion. This lotion acts as a barrier repair compound for those suffering from atopic dermatitis. Additionally, there are potential benefits as an antiaging agent in those with photodamage. The functional ingredients are incorporated into a propriety liposomal delivery system, creating this novel compound. One ingredient is derived from *Evodia rutaecarpa*, a tree used in traditional Chinese herbal medicine, with known properties as a skin-smoothing agent.[6] Another ingredient is the natural occurring amino acid L-ergothioneine, a known powerful antioxidant that scavenges reactive oxygen species (ROS), which play a major role in oxidative damage of the skin and the associated photodamage that occurs over time. This natural antioxidant has been shown to be effective in an in vitro skin model for photodamaged skin and is part of the novel barrier repair product to strengthen the skin against the formation of ROS.[7] The novel barrier repair product also contains liposomes that encapsule ursolic acid, a natural triterpenoid that is purified from rosemary leaves. Ursolic acid acts by prompting epidermal cells to produce ceramide lipids,[8] counteracting the appearance of skin aging. These liposomes have been shown to stimulate the production of ceramides in the skin of human subjects.[9] In addition, a lotion containing liposomes encapsulating ursolic acid, already studied, produced an increase in skin barrier repair function as evaluated by decreases in transepidermal water loss (TEWL).[10] In addition, a stabilized form of retinol, a highly reactive form of vitamin A found in many cosmeceutical products, is also included. Retinol is well recognized for its ability to increase the skin's own production of collagen and to improve the appearance of photoaging.[11] Retinol is both an essential vitamin and an antiaging treatment. The minimum dosage required for the antiaging effects and the associated exfoliation is approximately 0.4%. The amount of retinol in the novel barrier repair product is less than 0.05%, therefore it would not be truthful to call this product a retinol product in a base cream. However, low levels of vitamin A (retinol) serve to normalize skin function. This is particularly important in diseases with abnormal hyperproliferation that have been found to be deficient in vitamin A.[12]

The novel barrier repair product utilizes the unique nature and pH sensitivities of the liposomes and retinol packaged in propriety, patented liposome vehicles. These liposomes then carry the active ingredients into the uppermost layers of the skin.[13] This combination thus improves epidermal barrier function.

The present study looks to further evaluate this novel barrier repair product in improving the signs and symptoms of patients suffering from atopic dermatitis, with active atopic dermatitis in the antecubital fossa in individuals over a 28-day period of time.

MATERIALS AND METHODS

This clinical study was approved by an institutional review board and informed consents were obtained by all individuals participating in this clinical trial. Good Clinical Practice guidelines were followed during the entire course of this clinical trial.

In this clinical trial, 6 subjects were to be selected to participate. These subjects were healthy, normal volunteers between the ages of 12 and 65 years of age, with moderate and similar signs of atopic dermatitis in both of the antecubital fossa. Patients enrolled had to meet inclusion and exclusion criteria for this clinical trial, including having stable atopic dermatitis, not having used any topical or systemic therapy for atopic dermatitis for 2 weeks prior to patient enrollment (except for moisturization), and no evidence of active infection at the treatment site.

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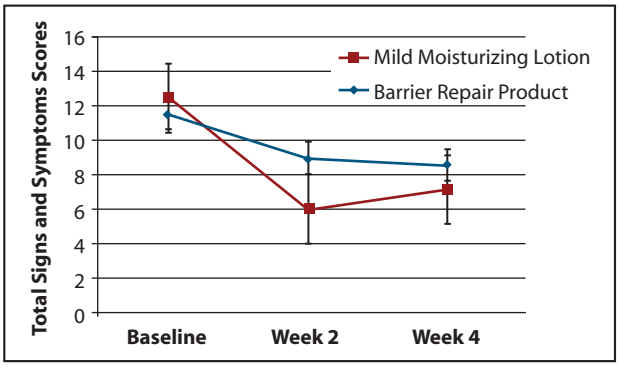

Figure 1. The average total signs and symptoms scores of a 28-day trial comparing a novel barrier repair product with a mild moisturizing lotion.

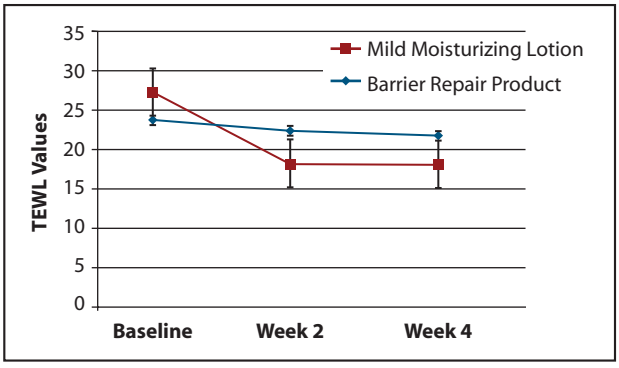

Figure 2. The average transepidermal water loss (TEWL) values of a 28-day trial comparing a novel barrier repair product with a mild moisturizing lotion.

Patients were randomized to which antecubital fossa to apply the blinded study products. One antecubital fossa was randomized to receive the novel barrier repair product, whereas the contralateral antecubital fossa was randomized to receive a mild moisturizing lotion. Each patient was instructed to apply each of the blinded products twice daily to the affected areas, with a designated amount of 2 mg/cm for each application.

At days 14 and 28, the subjects were evaluated for signs and symptoms of atopic dermatitis. These included evaluation of erythema, edema, lichenification, and excoriation utilizing a scale of 0.0 to 3.0, where 0.0 indicates absent signs and 3.0 indicates severe signs. Pruritus was measured on a scale of 0 to 10, where 0 indicates no pruritus and 10 indicates the worst pruritus. Quality of life was also evaluated, where 0 indicates no quality of life; 1, mild; 2, moderate; and 3, high. Also evaluated was TEWL on the ventral forearm at baseline and at days 14 and 28 utilizing an evaporimeter. Photographs and TEWL measurements were obtained. Because this was a pilot study, the sum of the signs and symptoms scores and the TEWL values were analyzed using a 1-tailed paired student's *t*-test.

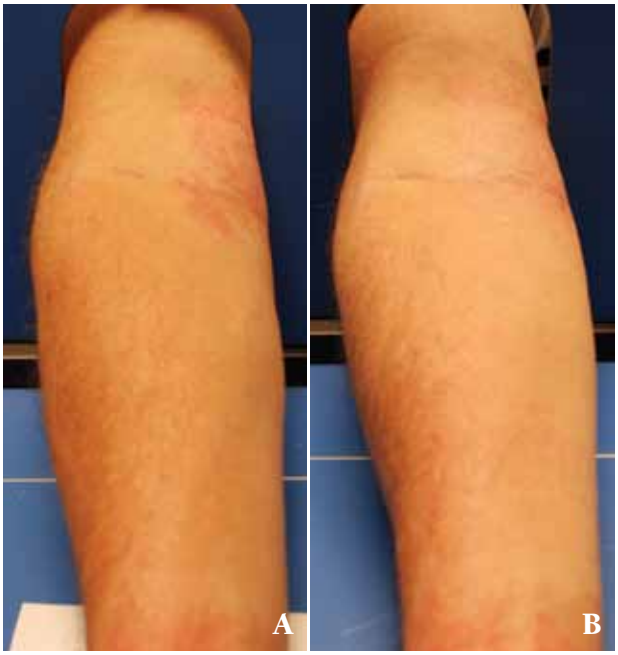

Figure 3. A 25-year-old male with atopic dermatitis at baseline (A) and after 2 weeks of treatment with a barrier repair product, with noticeable improvement (B).

RESULTS

Of the 6 individuals who were enrolled into this clinical trial, 5 of them completed it. One patient discontinued participation before the first evaluation due to intolerance to both study products. Of the 5 for whom efficacy data was available, there were 4 males and 1 female with an age range of 13 to 51 years.

In all of the study parameters, the novel barrier repair product showed an improvement over the mild moisturizing lotion. Nearly all of the improvement occurred during the initial 2 weeks of treatment. The total signs and symptoms scores for this clinical trial are shown in Figure 1. By the end of the second week of treatment, the novel barrier repair product was found to be significantly superior ($P<.05$). The changes in TEWL are shown in Figure 2. By the end of the second week, the novel barrier repair product tended to be superior ($P<.10$) to the mild moisturizing lotion with regard to decreases in TEWL.

The following case highlights the results seen within this clinical trial (Figure 3). The patient who presented was a 25-year-old male. By the end of the second week of treatment, the total sign and symptom score on the side treated with the novel barrier repair product was 49.2% of that on the side treated with the mild moisturizing lotion, and the TEWL value was 25.5%.

CONCLUSIONS

Although there was only a small sample of patients in this clinical trial, the results achieved were very encouraging

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and showed the effectiveness of the novel barrier repair product in combating the signs and symptoms of patients suffering from moderate atopic dermatitis. The effects of the product with regard to TEWL tended to show the improvement in barrier function, which can be achieved through this unique combination of products found in this novel compound. The combination of *E rutaecarpa*, a naturally occurring amino acid, liposomes containing ursolic acid, and a stabilized form of retinol in a propriety liposomal delivery system should be considered useful in patients suffering from atopic dermatitis and warrants further clinical investigations in a larger patient population and in association with other medications routinely utilized in patients suffering from atopic dermatitis to further maximize the potential of this unique compound.

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