Barrier Products May Play Role in Dermatitis Tx

Products can improve skin hydration and decrease barrier dysfunction, but more studies are needed.

BY DOUG BRUNK
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SAN DIEGO — Barrier products may play a role as adjuvant therapy for patients with atopic dermatitis, but better studies are needed to demonstrate their efficacy.

That's the conclusion Dr. Andrew C. Krakowski made about three barrier products he discussed at a meeting on skin disorders sponsored by Rady Children's Hospital: palmitamide monoethanolamine (PEA) nonsteroidal cream (MimyX), hydrolipidic cream MAS063DP (Atopiclair), and ceramide-based emulsion (EpiCeram).

These products are 510(k) medical devices that have been cleared for marketing by the Food and Drug Administration. The manufacturers claim that they contain ingredients that might help to replace normal epidermal lipids, improve skin hydration, decrease skin barrier dysfunction, and relieve the atopic dermatitis symptoms of stinging, burning, and pruritus.

Such features are important, Dr. Krakowski said, because "we know that barrier dysfunction correlates with atopic dermatitis severity and we think there is a possible increased allergy absorption that happens through the skin of our atopic dermatitis patients. We also know that atopic dermatitis skin is a great setup for microbial colonization, and that puts you at increased risk of secondary infection. We also have good data that a disrepaired skin barrier leads to increased transepidermal water loss."

There are several barrier products currently on the market, but he limited his discussion to the three that have been studied recently:

► **EpiCeram.** Licensed by the University of California and manufactured by Ceragenix Pharmaceuticals Inc., EpiCeram is a combination of ceramides, cholesterols, and fatty acids that is expected to hit the U.S. market this fall, said Dr. Krakowski. The current cost is not known.

In a multicenter, randomized study sponsored by Ceragenix and presented as a poster at the 2008 annual meeting of the Society of Pediatric Dermatology, investigators compared 4 weeks of twice-daily ceramide-based emulsion to fluticasone propionate in children with moderate to severe atopic dermatitis. (See related story below.)

On day 14, subjects in the fluticasone group had significantly better Scoring Atopic Dermatitis (SCORAD) scores, compared with those in the ceramide-based emulsion group. By day 28, there were no significant differences in SCORAD scores between the two groups.

'The cost of these products needs to be reconciled with their cost-effectiveness; most of these products may not be covered by insurance.'

In a second multicenter, randomized study that included patients from Rady Children's Hospital, investigators compared 4 weeks of twice-daily ceramide-based emulsion to pimecrolimus in 38 pediatric subjects with mild to moderate atopic dermatitis. No intention-to-treat analysis was performed.

Subjects in both groups demonstrated significant improvement in Investigator Global Assessment (IGA) scores at days 14 and 28. "There was also no significant difference in pruritus between the two groups, but it wasn't clear if there was any improvement," said Dr. Krakowski, a first-year dermatology resident at the University of California, San Diego.

Subjects in the ceramide-based emulsion group had no significant improvement from baseline in Eczema Area and Severity Index (EASI) scores. By day 14, subjects in the pimecrolimus group had significantly better EASI scores, compared with their counterparts in the ceramide emulsion group. By day 28, there were no differences in median score reductions between the groups.

► **MimyX.** Manufactured by Stiefel Laboratories Inc., this water-based product is described as a fragrance-, dye-, and preservative-free emulsion to be used three times a day or as needed. According to the manufacturer's Web site, it comes as a 140-g tube, with a cost of $101, or about $22 per ounce.

The main ingredient is PEA, which is found naturally in the stratum granulosum and is thought to downregulate inflammatory response. "It's a cannabinoid agonist that is believed to modulate mast cells and immune cells, theoretically reducing histamines, cytokines, and IL-4, -6, and -8," Dr. Krakowski added. "It's also thought to bind CB2 receptors on cutaneous nerves and decrease the transmission of pruritus."

In an international open-label study, investigators assessed the effects of the PEA nonsteroidal cream applied at least twice daily for 38 days in 2,456 patients with mild to moderate atopic dermatitis (J. Eur. Acad. Dermatol. Venereol. 2008;22:73-82). Of the 2,456 patients, 923 were 12 years of age or younger.

By the end of the study, physician assessment scores demonstrated that pruritus improved by 56%, erythema by 54%, dryness by 57%, lichenification by 55%, and excoriations by 63%.

The investigators also found that by the end of the treatment period, 63% of children reduced their use of topical corticosteroids, compared with 53% of adults. In addition, 34% of subjects were able to stop using their topical corticosteroid altogether and 12% were able to switch to a lower-potency steroid.

► **Atopiclair.** Manufactured by Graceway Pharmaceuticals LLC, this product contains hyaluronic acid, *Vitis vinifera* (grape leaf extract), telmesteine, glycyrrhetinic acid (licorice extract), and shea butter, a derivative of shea nut oil. The product is described as dye- and fragrance-free and is used 2-3 times per day or as needed. It comes in a 100-g tube and costs about $34 per ounce.

In a multicenter, randomized, double-blind, vehicle-controlled trial, 106 infants and children with mild to moderate atopic dermatitis applied hydrolipidic cream MAS063DP or vehicle three times a day to past, current, or "reasonable future" sites as monotherapy for 43 days (J. Pediatr. 2008;152:854-9). The mean age of subjects was 5 years.

One target lesion was chosen by investigators for evaluation and photography (mostly identified on extremities). Success was defined as reaching an IGA score of 0 (clear) or 1 (almost clear).

In an intention-to-treat analysis, 53 of 69 subjects (77%) in the hydrolipidic cream group achieved a score of 0 or 1 at day 22, compared with none in the vehicle group. "The vehicle used in the study wasn't your normal petrolatum vehicle," Dr. Krakowski noted. "It was the vehicle the hydrolipidic cream came in."

Pruritus, EASI scores, subject and caregiver assessment of global response, onset and duration of itch relief, and need for rescue medication were all significantly improved in the treatment group, compared with the vehicle group.

"I think barrier products could be helpful as adjuvant treatment for atopic dermatitis," he commented. " I think the cost of these products needs to be reconciled with their cost-effectiveness; most of these products may not be covered by insurance. We also need better head-to-head, long-term, pediatric-specific trials to demonstrate efficacy of these products for treating flares directly and for maintenance therapy over the long term."

Dr. Krakowski disclosed having had no relevant conflicts of interest. ■

More on the Effectiveness of EpiCeram for Atopic Dermatitis

BY BRUCE JANCIN
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KYOTO, JAPAN — Topical EpiCeram is an effective stand-alone therapy for moderate to severe pediatric atopic dermatitis, according to results of a clinical trial.

This physiologic skin barrier repair cream proved itself the equal of fluticasone proprionate cream (Cutivate) in a 113-patient multicenter randomized head-to-head comparison, Dr. Jeffrey L. Sugarman reported at an international investigative dermatology meeting.

The observed improvement with EpiCeram in clinical disease severity scores was not as fast as with the mid-strength topical steroid. However, by the conclusion of the 4-week, investigator-blinded trial the two groups showed statistically and clinically similar gains in the Scoring Atopic Dermatitis (SCORAD) index, itching scores, and sleep habits, said Dr. Sugarman, a dermatologist in private practice in Santa Rosa, Calif., and at the University of California, San Francisco.

"I think EpiCeram is an important advance in the management of atopic dermatitis," he said in an interview at the meeting of the European Society for Dermatological Research, the Japanese Society for Investigative Dermatology, and the Society for Investigative Dermatology.

"It's a well thought-out barrier cream that utilizes our current understanding of the skin barrier in atopic dermatitis in its design and formulation," he added.

Indeed, EpiCeram is emblematic of a new paradigm in atopic dermatitis therapy that is based upon targeted, disease-specific lipid replacement, with a resultant marked reduction in the need for topical steroids or immunomodulators. The aim is to repair defective skin barrier function. This is in line with current thinking regarding the pathogenesis of atopic dermatitis, which holds that defective barrier function is the driver of disease activity rather than a consequence of an underlying immunologic defect, Dr. Sugarman continued.

The 113 participants in the clinical trial ranged in age from 6 months to 18 years. From a mean baseline SCORAD of 36, the EpiCeram-treated group showed a 47% improvement after 2 weeks and a 57% improvement after 4 weeks. The 4-week gain was statistically similar to the mean 69% improvement after 4 weeks of fluticasone, although the mean 61% improvement in SCORAD after 2 weeks of fluticasone was significantly better than with EpiCeram at that time point.

After 2 weeks of twice-daily therapy, only 4% of patients in the EpiCeram group showed a greater than 75% improvement in SCORAD scores, compared with 20% on fluticasone. By 4 weeks, 21% of EpiCeram-treated patients had exceeded this threshold, similar to the 26% rate in the fluticasone group.

Pruritis scores improved from a mean baseline of 6.1 on a 10-point scale to 3.5 with EpiCeram and 3.7 with fluticasone after 4 weeks. Sleep habits also improved significantly from a mean baseline of 3.5 on a 10-point scale to 2.6 with EpiCeram and 2.8 with fluticasone.

The study was sponsored by Ceregenix Corp., which has received Food and Drug Administration marketing approval for EpiCeram. Dr. Sugarman indicated he has no financial relationship with the company.

Ceregenix has granted exclusive EpiCeram distribution and marketing rights in the United States to Dr. Reddy's Laboratories Ltd., which plans to launch the prescription cream this fall. ■