Data Sought on Atopic Dermatitis Barrier Products

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Barrier products may play a role as adjuvant therapy for patients with atopic dermatitis, but better studies are needed to show how they fit into the armamentarium.

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

The products are 510(k) medical devices that have been cleared for marketing by the Food and Drug Administration. The manufacturers claim they contain ingredients that might help 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, because "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 dermatitic patients," said Dr. Krakowski. "Atopic dermatitis skin is a great setup for microbial colonization, and that puts you at increased risk of secondary infection."

There are several barrier products on the market, but Dr. Krakowski focused on the three that have been studied recently:

► **EpiCeram.** A combination of ceramides, cholesterols, and fatty acids, Epiceram has been licensed by the University of California and manufactured by Ceragenix Pharmaceuticals Inc.

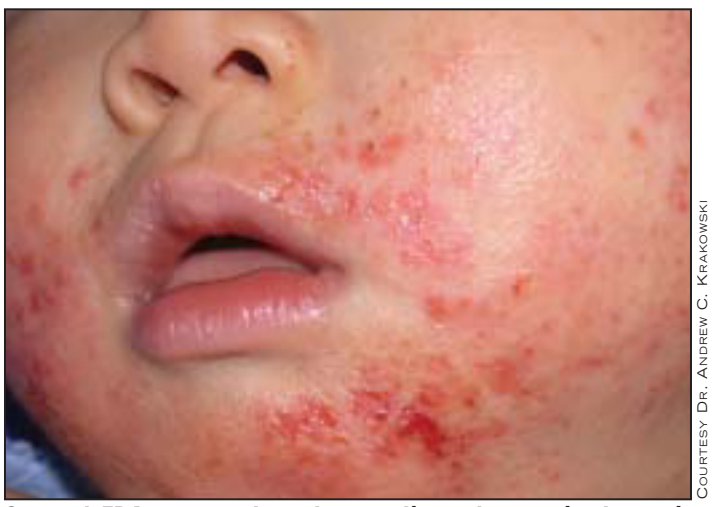
In a multicenter, randomized study sponsored by Ceragenix and presented during a poster session at the 2008 annual meeting of the Society of Pediatric Dermatology, investigators compared 4 weeks of twice-daily ceramide-based emulsion with fluticasone propionate in 121 pediatric subjects with moderate to severe atopic dermatitis.

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

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 scores at day 14 and day 28. "There was also no significant difference in pruritus between the two groups, but it wasn't clear if there was any improvement from baseline," said Dr. Krakowski, a pediatrician and 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.



COURTESY DR. ANDREW C. KRAKOWSKI

Several FDA-approved products relieve the atopic dermatitis symptoms of stinging, burning, and pruritus.

► **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 company'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.

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, 12% were able to switch to a lower-potency steroid, and 3% switched to a high-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.

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

Think Efficacy and Toxicity in Selecting Psoriasis Medications

BY KERRI WACHTER
Senior Writer

PARIS — Nonbiologic systemic drugs can be effective choices for the treatment of psoriasis if they are chosen properly, according to Dr. Jonathan Barker.

"The important message is that standard, traditional systemic drugs work," said Dr. Barker at the annual congress of the European Academy of Dermatology and Venereology. However, these drugs are not always effective and are often associated with considerable toxicity.

"To optimize systemic therapy, we're talking about maximizing efficacy and minimizing toxicity," said Dr. Barker, head of the skin inflammation unit at St. John's Institute of Dermatology, King's College, London, who gave an overview of several standard systemic drugs.

► **Methotrexate.** The preferred drug for unrelenting disease that is likely to require long-term therapy, it is also effective for treating psoriatic arthritis said Dr. Barker. The key to avoiding adverse events with the drug is to start with a low dose and increase it slowly.

Dr. Barker said he and his colleagues begin psoriasis patients on 5 mg/week and increase the dose by 5 mg/week up to 15 mg for the first 3 months. The maximum dose they use for psoriasis patients is 25 mg.

It's not commonly recognized that most causes of death that are associated with methotrexate are attributable to bone marrow suppression, not hepatotoxicity. These deaths are usually a result of some confusion over the dosing regimen or folic acid deficiency, he said. Bone marrow suppression is rare when patients are on folic acid supplementation.

Dr. Barker noted that it is possible to monitor liver function without routine liver biopsy by monitoring serum procollagen III aminopeptide (Br. J. Dermatol. 2005;152:444-50). For his psoriasis patients on long-term methotrexate, he checks serum procollagen III aminopeptide every 3 months.

"If this practice were to be widely adopted, then methotrexate would become a more acceptable option for many patients who are dissuaded from considering it because of the threat of repeated liver biopsy," he said.

► **Cyclosporine.** It is a fast-acting drug that "presents a different set of problems with respect to usage," Dr. Barker noted. "It's a very good drug for patients with intermittent disease, where they need a quick fix but you're hoping that the duration of therapy will be very short."

Glomerular sclerosis is extremely unlikely to occur in patients who are treated with cyclosporine for less than 12 months and in whom there is an insignificant rise in creatinine levels. Glomerular sclerosis is much more likely to occur when cyclosporine is used for more than a year.

In addition, long-term cyclosporine A—the main form of this drug—is associated with an increased risk of nonmelanoma skin cancer. However, this risk can be minimized by limiting both dosage and duration of use (no longer than 1-2 years), said Dr. Barker. Cyclosporine use should be minimized in patients who have had significant phototherapy.

► **Acitretin.** It can be used "occasionally in moderate chronic plaque psoriasis, more so in palmo-plantar pustulosis," said Dr. Barker, who added that he starts with the lowest dosage (25 mg/day) and uses it with narrow-band UVB phototherapy.

However, one should use extreme caution when treating women of child-bearing age with acitretin because it can cause major fetal abnormalities, he cautioned.

In addition, it is very helpful as an adjunctive treatment for patients with severe disease and multiple squamoproliferative lesions who have been on phototherapy in the past.

"This is not an immunosuppressive drug and there is some evidence that it has chemoprotective activity for malignancy," he said.

Dr. Barker has consulted for several pharmaceutical companies making biologics but noted that none was relevant to his presentation. ■