Non-steroidal, Antifungal, Anti-inflammatory Cream for Seborrheic Dermatitis

Suitable for use as monotherapy or an as adjunct to traditional therapies, a new formulation provides more options in the management of this somewhat common condition.

By Joseph Bikowski, MD

Seborrheic dermatitis, while not typically associated with excessive physical discomfort, may produce pruritus and is associated with significant potential impact on a patient's appearance, self-image,[1] and quality of life.[2] As such, many affected patients desire to achieve clear skin but are not willing to submit to a therapy that may cause discomfort or pose risks of adverse events. A number of available effective treatments are generally patient-friendly and safe, although they each have limitations. A novel non-steroidal, anti-inflammatory cream offers another option, either alone or in combination, for management of this somewhat common condition.

Typical Approaches

Standard interventions for seborrheic dermatitis, which is found to affect up to five percent of the population,[3] include topical steroids, topical immune modulators (TIMs) tacrolimus and pimecrolimus, azoles and other antifungals, and keratolytic agents. Seborrheic dermatitis, characterized by flaking, erythema, and pruritus, is most common in infants up to three months of age and adults age 30 to 60.[3] It affects men more frequently than women and may present concomitantly with other common cutaneous diseases like acne and rosacea. Although the exact etiology of SD is not well elucidated, the *Malassezia* yeast is thought to play a role. In addition, increased sebaceous and androgenic activity have been implicated.[3]

Topical azole antifungals, which are active against *Malassezia* and also confer limited anti-inflammatory effects[4] tend to be first-line antifungal options for SD management. Topical allylamines, benzylamines, and hydroxypyridones have been used as well, while for widespread involvement, oral ketoconazole, itraconazole, or terbinafine may be indicated.[4] However, because anti-inflammatory effects of anti-fungals are limited, significant

improvement in SD symptoms may be slow to emerge. Therefore, topical antifungals are often used in combination with anti-inflammatory agents.

While topical corticosteroids are shown to reduce the inflammation and associated erythema of SD, they do not confer antifungal effects. They may be associated with unsatisfactory rates of recurrence, so are often used in combination with antifungal treatments.[5] Furthermore, use of corticosteroids on the face requires particular caution due to associated risks, such as atrophy and telangiectases.

Relatively recently, topical immune modulators, tacrolimus and pimecrolimus, have been adopted for use in SD treatment. These are shown to reduce inflammation and erythema in patients with SD in as little as two weeks.[6] Unlike corticosteroids, they are not associated with risk of atrophy and are generally considered safe for longer courses of therapy, however they are not approved for use in children under two, and they carry a boxed warning. They may also be associated with problematic rates of recurrence, although data suggest recurrent presentations are less severe than following corticosteroid treatment.[6]

Keratolytic agents are commonly used adjunctively in acute and maintenance therapy to reduce scaling and flaking, though they do not directly affect inflammation and erythema. They are also commonly used as maintenance therapy. Topical azelaic acid is another option for management, as it confers anti-inflammatory, antifungal, and keratolytic effects.[3] Its use in SD has clinical and anecdotal support but no published controlled trials currently.

A new non-steroidal cream formulation (Promiseb Cream, Promius Pharma) has recently received FDA clearance for management of the symptoms of SD, including itching, erythema, scaling, and pain, and it may be a suitable monotherapy or adjunctive treatment option for a majority of SD patients.

The Evidence

Due to the novelty of the product, published studies for Promiseb Cream are limited, however four studies provide evidence of the benefits of the formulation. The first was a head-to-head comparison of Promiseb Cream to desonide cream 0.05% for management of the inflammatory symptoms of facial SD. Of 77 subjects with facial SD enrolled in the randomized, investigator-blinded study, 34 individuals completed the Promiseb Cream arm and 38 completed the desonide cream arm.[7] Subjects applied the assigned treatment twice daily for 14 days. Those who were clear discontinued therapy at day 14, others continued application of the same therapy for up to 14 additional days. Patients ranged in age from 21 to 85 with a mean of 52 years. Nearly three-quarters of subjects were men, and 30 percent were non-whites.

On a scale of 0-3, (0 = clear, 1 = almost clear, 2 = mild, 3 = moderate), mean baseline scores for Investigator Global Assessment were 2.5. At days 14 and 28, patients treated with Promiseb Cream and desonide cream 0.05% demonstrated a statistically significant reduction in IGA mean score from baseline ($P < .0001$). There was no statistically significant difference in improvement in IGA between treatments at day 14 or day 28 ($P > .2$). At day 14, 18 percent of the Promiseb Cream patients were rated clear by Investigator Global Assessment, and 36 percent of the desonide cream patients were clear. There was a statistically significant difference in relapse rates between the two groups, with 71 percent of all Promiseb Cream patients remaining clear at day 28 compared to only 14 percent of desonide cream patients. Looked at another way, the relapse rate was 29 percent for Promiseb Cream compared to 86 percent for desonide cream. Although the differences in the treatment groups were not significant, at day 28 a greater proportion of patients in the Promiseb Cream group were clear (51 percent) than in the desonide cream group (41 percent). On a scale of 0-3 (0 = none, 1 = slight, 2 = mild, 3 = moderate), average baseline scores for erythema and scaling were approximately 2.5 and pruritus was approximately 2 for both treatment groups. At days 14 and 28, both treatment groups demonstrated statistically significant reduction from baseline for erythema, scaling and pruritus, with no statistically significant difference between treatment groups. Adverse events were minimal for the two groups. The PI for Promiseb Cream cautions against its use by patients with a known allergy to any of its ingredients,

including shea nut butter, nuts and nut oil, which did not appear to be a problem in this study.

Another study, which assessed patient acceptance of Promiseb, found high levels of patient acceptance. The study involved an active group that used Promiseb Cream (n = 40) and controls (n = 20) who used vehicle (comprised of the four primary base ingredients). In terms of patient satisfaction, 85 percent of treated patients wanted to (64 percent) or were likely to (21 percent) continue using Promiseb, and 97 percent found the product easy or very easy to spread. All treated patients reported that Promiseb Cream had a pleasant odor (26 percent), an acceptable odor (38 percent), or no odor at all (36 percent).

A third study measured the antifungal activity of Promiseb Cream against *Malassezia* yeasts. The study involved 10 healthy adult volunteers whose fungal load was measured at two target sites on the chest.[7] A sample was taken by tape stripping from each site at baseline and placed on an agar plate. Then, patients treated one designated site with a pea-sized amount of Promiseb Cream twice daily for seven days. The untreated site was the control. Again, a tape-strip sample was taken from each site, and counts were taken after seven days. At baseline, seven of 10 patients were positive for *Malassezia* (counts ranged from one to 195 per tape). After treatment, there was a 94 percent reduction in *Malassezia* colonies at treated sites compared to a 49 percent reduction at control sites. This was a statistically significant difference.

A study in guinea pigs further demonstrated Promiseb Cream's antifungal activity relative to an established antifungal therapy after three days of treatment. This was a four-arm study in which all animals were infected with *M. furfur* for seven consecutive days. One control group (n = 4) was cultured at day seven. A second control group (n = 8) was cultured on day 10. A third group (n = 8) received topical ciclopirox olamine 0.77% cream once daily on days 8-10. The fourth group (n = 8) received Promiseb Cream was applied once daily on days 8-10. Groups 2, 3, and 4 were cultured on day 11. Whereas all of the samples from the control groups were positive for colonization at day 11, none of the treated group samples were.

An Alternative and an Adjunct

Despite the availability of multiple treatment options for SD, clinicians and patients are both interested in alternative options that may enhance patient safety and satisfaction. Steroid-free Promiseb Cream is a useful new addition to the treatment palette. The product's fast-acting anti-inflammatory action, shown to be similar to that of desonide 0.05%, may obviate the need for topical corticosteroids in management of mild to moderate SD. Promiseb Cream presents a suitable alternative to slower-acting TIMs, which may be contraindicated in the youngest SD patients (under age two).

Promiseb Cream may be used as a first-line therapeutic and maintenance agent for patients with mild SD as a replacement for topical steroids and topical antifungal products. In addition to its corticosteroid-sparing role, the anti-fungal activity of Promiseb may permit dermatologists to decrease their reliance on topical antifungal agents.

When necessary for moderate presentations or in the case of recurrent mild SD, topical antifungals or topical corticosteroids may be used in conjunction with Promiseb Cream. With its favorable safety profile and high level of patient acceptance, Promiseb may be used indefinitely as a maintenance therapy if patients desire. Alternatively, patients can be instructed to begin applying the cream at the first sign of a flare. Theoretically, this will decrease the rate of progression to more significant involvement and further reduce the need for antifungal and other therapeutic agents. ■ ☑

Dr. Bikowski is a consultant and has served on the Advisory Board and Speakers Bureau for Promius Pharma.

1 Naldi L, Rebora A. Clinical practice. Seborrheic dermatitis. N Engl J Med. 2009;360(4):387-96.

2 Szepietowski JC, Reich A, et al. Quality of life in patients suffering from seborrheic dermatitis: influence of age, gender and education level. Mycoses. 2008 Sep 12.

3 Bikowski J. Facial seborrheic dermatitis: a report on current status and therapeutic horizons. J Drugs Dermatol. 2009 Feb;8(2):125-33.

4 Gupta AK, Nicol K, Batra R. Role of antifungal agents in the treatment of seborrheic dermatitis. Am J Clin Dermatol. 2004;5(6):417-22

5 Elewski BE. Safe and effective treatment of seborrheic dermatitis. Cutis. 2009;83(6):333-8.

6 Cook BA, Warshaw EM. Role of topical calcineurin inhibitors in the treatment of seborrheic dermatitis: a review of pathophysiology, safety, & efficacy. Am J Clin Dermatol. 2009;10(2):103-18.

7 Data on file, Promius Pharma, LLC.