What's New in Topical Treatments for Psoriasis

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In an era when we have access to a dizzying array of biologics for psoriasis treatment, it is easy to forget that topical therapies are still the bread and butter of treatment. For the majority of patients living with psoriasis, topical treatment is the only therapy they receive; indeed, a recent study examining a large national payer database found that 86% of psoriasis patients were managed with topical medications only.[1] Thus, it is extremely important to understand how to optimize topical treatments, recognize pitfalls in management, and utilize newer agents that can been added to our treatment armamentarium for psoriasis.

In general, steroids have been the mainstay of topical treatment of psoriasis. Their broad anti-inflammatory activity works well against both the visible signs and symptoms of psoriasis as well as the underlying inflammatory milieu of the disease; however, these treatments are not without their downsides. Hypothalamic-pituitary-adrenal (HPA) axis suppression, especially in higher-potency topical steroids, is a serious concern that limits their use. In one study comparing lotion and cream formulations of clobetasol propionate, HPA axis suppression was seen in 80% (8/10) of adults in the lotion group and 30% (3/10) in the cream group after 4 weeks of treatment.[2] These findings are not new; a 1987 study found that patients using less than 50 g of topical clobetasol per week, which is considered a low dose, could still exhibit HPA axis suppression.[3] Severe HPA axis suppression may occur; one study of various topical steroids found some degree of HPA axis suppression in 38% (19/50) of patients, with a direct correlation with topical steroid potency.[4] Additionally, cutaneous side effects such as striae formation, atrophy, and the possibility of tachyphylaxis must be considered. Various treatment regimens have been developed to limit topical steroid use, including steroid-sparing medications (eg, calcipotriene) used in conjunction with topical steroids, systemic treatments (eg, phototherapy) added on, or higher-potency topical steroids rotated with lower-potency steroids. Implementing other agents, such as topical retinoids or keratolytics, into the treatment regimen also is an important consideration in the overall approach to topical psoriasis therapy.

Notably, a number of newly approved topical treatments for psoriasis have emerged, and more are in the pipeline. When evaluating these agents, important considerations include safety, length of treatment course, and efficacy. Several of these agents hold promise for patients with psoriasis.

An alcohol-free, fixed-combination aerosol foam formulation of calcipotriene 0.005% and betamethasone dipropionate 0.064% was approved by the US Food and Drug Administration for plaque psoriasis in 2015. This agent was shown to be more efficacious than the same combination of active ingredients in an ointment formulation as well as either agent alone, with psoriasis area and severity index 75 response achieved in more than 50% of patients at week 4 of treatment.[5] Notably, this product offers once-daily application with positive patient satisfaction scores.[6] The novelty of this foam is in its ability to supersaturate the active ingredients on the surface of the skin with improved penetration and drug delivery.

A novel spray formulation of betamethasone dipropionate 0.05% also has been developed and has been compared to augmented betamethasone dipropionate lotion. One benefit of this spray is that, based on the vasoconstriction test, the potency is similar to a mid-potency steroid while the efficacy is not significantly different from betamethasone dipropionate lotion, a class I steroid.[7] Hypothalamic-pituitary-adrenal axis suppression was similar following a 4-week treatment course compared to a 2-week course of the lotion formulation.[8]

The newest agent, halobetasol propionate lotion 0.01%, was approved for treatment of psoriasis in October 2018. Compared to halobetasol 0.05% cream or ointment, halobetasol propionate lotion 0.01% has one-fifth the concentration of the active ingredient with the same degree of success in efficacy scores.[9] This reduction in drug concentration is possible because the proprietary lotion

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base allows for better drug delivery of the active ingredient. Importantly, HPA axis suppression was assessed over an 8-week period of use and no suppression was noted.[9] Generic class I steroids should only be used for 2 weeks, which is the standard treatment period used in comparator trials; however, many patients will still have active lesions on their body after 2 weeks of treatment, and if using generic clobetasol or betamethasone dipropionate, the choice becomes whether to keep applying the medication and risk HPA axis suppression and cutaneous side effects or switch to a less effective treatment. However, some of the newer agents are indicated for 4 to 8 weeks of treatment.

Utilizing other classes of agents such as retinoids and keratolytics in our treatment armamentarium for psoriasis often is helpful. It has long been known that tazarotene can be combined with topical steroids for increased efficacy and limitation of the irritating effects of the retinoid.[10] Similarly, keratolytics play a role in allowing a topically applied medication to penetrate deep enough to affect the underlying inflammation of psoriasis. Medications that include salicylic acid or urea may help to remove ostraceous scales from thick psoriasis lesions that would otherwise prevent delivery of topical steroids to achieve clinically meaningful results. For scalp psoriasis, there are salicylic acid solutions as well as newer agents such as a dimethicone-based topical product.[11]

Nonsteroidal topical anti-inflammatories also have been used off label for psoriasis treatment. These agents are especially useful in patients who were not successfully treated with calcipotriene or need adjunctive therapy. Although not extremely effective against plaque psoriasis, topical tacrolimus in particular seems to have a place in the treatment of inverse psoriasis where it can be utilized without concern for long-term side effects.[12] Crisaborole ointment, a topical medication approved for treatment of atopic dermatitis, was studied in phase 2 trials, but development has not progressed for a psoriasis indication.[13] It is reasonable to consider this medication in the same way that tacrolimus has been used, however, considering that the mechanism of action—phosphodiesterase type 4 inhibition—has successfully been implemented in an oral medication to treat psoriasis, apremilast.

There are numerous topical medications in the pipeline that are being developed to treat psoriasis. Of them, the most relevant is a fixed-dose combination of halobetasol propionate 0.01% and tazarotene 0.045% in a proprietary lotion vehicle. A decision from the US Food and Drug Administration is expected in the first quarter of 2019. This medication capitalizes on the aforementioned synergistic effects of tazarotene and a superpotent topical steroid to achieve improved efficacy. Similar to halobetasol lotion 0.01%, this product was evaluated over an 8-week period, and no HPA axis suppression was observed. Efficacy was significantly improved versus both placebo and either halobetasol or tazarotene alone.[14]

Overall, it is promising that after a long period of relative stagnancy, we have numerous new agents available and upcoming for the topical treatment of psoriasis. For the vast majority of patients, topical medications still represent the mainstay of treatment, and it is important that we have access to better, safer medications in this category.

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