Combination Approaches Using Topical Vitamin D for Psoriasis

A combination of topical vitamin D with some form of phototherapy and/or systemic therapy is a safe and effective option for plaque psoriasis.

**BY JERRY BAGEL, MD**

Psoriasis is a complex disease and therefore the use of combination therapy to optimize benefits and minimize risk is intuitive. With the right combination, the effect of each individual component can be maximized for optimal response. While topical therapy often forms the foundation of any combination, any number of possibilities involving oral, systemic, and even light-based options in conjunction with topical therapy may constitute an effective approach for plaque psoriasis. One particular emerging option combines topical vitamin D with phototherapy and systemic therapy.

Several studies have evaluated the potential benefits of differing variations of topical vitamin D analogues with phototherapy and systemic therapy separately and together. These studies may point to new directions in treatment. This article will review these studies and explore further how this specific combination might be beneficial for patients.

**REVIEWING THE DATA**

**Vitamin D Plus Phototherapy.** An eight-week study evaluated calcitriol 3ug/g ointment in combination with broadband UVB; 104 patients with a Body Surface Area (BSA) greater than or equal to 25 percent received UVB treatments on their entire body.1 Patients were also treated with white petrolatum on one half of the body and the other half with calcitriol ointment. In the calcitriol-treated patients, 45 percent cleared with a 65 percent improvement in PASI, whereas in the petrolatum side only 20 percent cleared with a 43 percent improvement in PASI. In addition, the calcitriol-treated side required 34 percent less UVB radiation than did the side to which petrolatum had been applied.

Another study evaluated 101 patients who received broadband UVB plus calcipotriol BID on one side of the body and on the other side received no UVB and only calcipotriol BID.2 The investigators found that 57 percent of patients were clear in the calcipotriol plus UVB group, as opposed to just 25 percent of patients in the calcipotriol-alone group.

Narrowband-UVB (NB-UVB) can also yield effective results in combination with calcipotriol. One study evaluated 50 patients, all of whom received NB-UVB treatment.3 In addition, 25 patients received calcipotriol BID and 25 patients were given emollient BID. By the 14th treatment, those in the calcipotriol group decreased by 75 percent in PASI, as compared to 55 percent in the emollient group. Additionally, only 18 treatments were necessary in the calcipotriol group, as opposed to 20 in the emollient group.

Psoralen plus UVA (PUVA) can also be combined effectively with topical vitamin D. A 10-week study in 2004...
evaluated calcipotriene cream and PUVA in 120 patients with a BSA greater than or equal to 30 percent. Findings showed that 87 percent of patients receiving PUVA three times per week plus calcipotriene achieved PASI 90, with a UVA dose of 99, as compared to just 47 percent of patients receiving PUVA plus placebo cream achieving PASI 90 with a UVA dose of 120.

Frappaz evaluated 110 patients combining PUVA with calcipotriol. The study involved a two-week washout period. During the second two weeks, patients were randomized to receive calcipotriol ointment or placebo. Then, in the third phase of the study, patients underwent 10 weeks of PUVA plus either calcipotriol or placebo. Patients in the calcipotriol group saw a PASI improvement of 91 percent, as opposed to 75 percent improvement for patients with placebo. Moreover, 87 percent of patients in the calcipotriol group achieved PASI 75, as compared to 64 percent of those in the placebo group.

Systemic Treatments Plus Vitamin D. Topical vitamin D and systemic combinations for psoriasis date back as far as 1994, when Grossman evaluated 69 patients over a six-week period comparing cyclosporine plus topical calcipotriol versus cyclosporine and placebo. Results showed that 50 percent of patients receiving the cyclosporine plus calcipotriol combination achieved PASI 90, with total improvement of 81 percent, as compared with just 12 percent of patients in the cyclosporine/placebo ointment group achieving PASI 90, and an overall improvement of 58 percent.

Calcipotriol has also been used in combination with acitretin. For example, Kerhof evaluated the effect of adding calcipotriol ointment to acitretin therapy in a 12-week study. All patients started on acitretin 20mg qd and were adjusted up to 70mg. Some patients then received calcipotriol, whereas others received a vehicle ointment. In the acitretin plus calcipotriol group, 67 percent of patients were fully clear, with a total of 73 percent improvement in PASI; total acitretin used was 1680mg. In the acitretin plus placebo group, 40 percent of patients were clear at the end of the study, with a total of 45 percent improvement in PASI; total acitretin used was 2100mg.

Another possible systemic combination methotrexate (MTX) along with topical vitamin D. One study evaluated MTX-treated patients given either calcipotriol or placebo ointment after cessation of MTX. At the time of relapse, MTX was resumed at 50 percent of the initial dose. No flares were reported in the calcipotriol group for 113 days, as compared to just 35 days to flare in the placebo group. The amount of MTX needed for improvement in the calcipotriol group was 6.5mg, as compared to 9.9mg in the placebo group.

Topical vitamin D can have an anti-inflammatory and anti-proliferative effects. Moreover, data suggest it may provide an additive benefit to the effects of phototherapy and systemic agents.

COMMENTARY
Psoriasis is a multi-factorial disease with various gene activities and different mechanisms controlling them. Vitamin D can be beneficial because it has immunomodulatory properties that decrease anti-microbial peptides seen in keratinocytes that promote the inflammatory process. Vitamin D is also involved in normal keratinization and can decrease the proliferative rate in the epidermis. Therefore, the benefit of topical vitamin D is two-fold: it can have both an anti-inflammatory and an anti-proliferative effect. Moreover, data suggest that it may provide an additive benefit to the effects of phototherapy and systemic agents. In addition, by using topical vitamin D in combination with these other therapies, clinicians can decrease the doses of either the light or systemic agent. In doing so, you can reduce the toxicity associated with the use of these agents as monotherapies. Thus, the potential benefits of a combination using topical vitamin D as a foundation can increase the efficacy and safety of all therapies.

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