Topical Vitamin D and Psoriasis Therapy

Data have shown that various forms of topical vitamin D in combination with existing therapies can enhance treatment outcomes and decrease the number of treatments.

By Jerry Bagel, MD

Although vitamin D is a sensitive subject in the dialogue about rising skin cancer rates, it deserves more attention on another end of the dermatology spectrum. The vitamin D derivative calcipotriol (or calcipotriene) is used for the treatment of mild to moderate psoriasis. With limited efficacy as stand-alone therapies, topical vitamin D therapies might be more effective when used in combination with existing psoriasis therapies, such as Narrowband UVB (NB-UVB), PUVA, acitretin, and methotrexate. Clinical studies show that the addition of vitamin D has resulted in an additive effect to these primary modalities. Vitamin D acts on a cellular level to enhance epidermal differentiation and to decrease hyperproliferation, resulting in greater benefit. This article explores the potential of vitamin D and consider the role it may play in the developing therapies for the treatment of psoriasis.

Light Therapy and Vitamin D

In one eight-week study, calcitriol 3ug/g ointment was used in combination with broadband UVB to treat plaque psoriasis. Patients received a reasonably aggressive dose of UVB (three times per week), with increasing doses depending on skin type. Half of the participants received UVB plus calcitriol, while the other half received UVB plus white petrolatum. After eight weeks, 45 percent of patients in the calcitriol group had clearance, with a PASI improvement of 65 percent, as compared to 20 percent clearance in the petrolatum group and a PASI improvement of 43 percent. Moreover, the calcitriol group required on average 34 percent less radiation than the white petrolatum group. Adverse events in the two groups were comparable, except for two cases of asymptomatic transient hypercalcemia in the calcitriol group.

Phototherapy (UVB) has also been administered in conjunction with topical calcipotriol. In the first of two trials (Series A), 101 patients were treated on one side with calcipotriol BID, and on the other with calcipotriol BID plus aggressive UVB light, and in the second (Series B), 81 patients were treated with UVB plus vehicle on one side, and with UVB plus calcipotriol BID on the other. Both series showed that calcipotriol plus UVB resulted in more effective and fewer treatments, with vast differences in Series A in overall clearance (52 percent in the calcipotriol plus UVB and 25 percent in the calcipotriol group).

Frappaz, et al. evaluated 110 patients with BSA between 20-50 percent. Half of the patients received calcipotriol ointment, the others received placebo; all received PUVA treatments three times per week for 10 weeks. PASI improvement in the PUVA plus calcipotriol group was 91 percent versus 75 percent in the placebo group. Patients in the PUVA/calcipotriol group required fewer light treatments to clear.

Another study found that patients using calcipotriene cream and undergoing aggressive PUVA therapy experienced significant PASI improvement as compared to patients receiving PUVA plus placebo. All patients had a total BSA between 20-50 percent, and after 10 weeks, in the combination group 69 percent of patients achieved PASI 90 with a total UVA dose of only 99 J, compared to 37 percent of controls at a total dose of UVA of 120 J.

Light therapy interaction. Several of these studies have recommended that the vitamin-based topi-
cal therapy not be applied within several hours of light therapy. One older study investigated this interaction. Patients applied calcipotriene ointment 0.005% five minutes prior to broadband UVB or PUVA therapy. After UV treatment, the ointment was removed and researchers measured the concentration of calcipotriene by reverse HPLC. Thin application of calcipotriene ointment failed to increase MED (UVB) or MPD (PUVA), but thick amounts of ointment resulted in increased MED (22.6 to 54.6 J/cm²) and MPD (20.2 to 24.5 J/cm²). While UVB did not change calcipotriene concentration, PUVA resulted in 28 percent reduction in calcipotriene concentration. The authors concluded that like salicylic acid and tar, calcipotriene may interfere with phototherapy; if applied immediately before phototherapy it can block UVB.

Therefore, it would seem prudent to apply calcipotriene ointment after UVA treatment to avoid possible loss of clinical efficacy. In vivo models with NB-UVB resulted in a dose-dependent decrease in calcipotriene concentration (250-1000 J/cm²). Patients who applied calcipotriene immediately after UVB experienced burning. Therefore, it is best to apply calcipotriene at least two hours after phototherapy.

Systemic Therapy and Vitamin D

Systemic therapy has also been used in conjunction with vitamin D topical products. In 1994, Grossman et al compared 2mg/kg cyclosporine plus calcipotriol ointment vs. 2mg/kg CsA plus placebo ointment for six weeks in 69 patients with an average PASI score of 25. Each group used approximately 70g of ointment per week, but the CsA plus calcipotriol ointment group experienced an overall PASI improvement of 81 percent, with 50 percent of patients achieving PASI 90. By comparison, the CsA plus placebo group experienced an average PASI improvement of 58 percent, with only 12 percent of patients achieving PASI 90.

Calcitriol was also used in conjunction with acitretin in a 12-week study. All patients started on 20mg acitretin QD and adjusted by 10mg QO week (max 70g). A total of 76 patients were registered to the calcitriol BID group and 59 patients to the vehicle ointment BID group. Sixty seven percent of patients in the calcitriol group experiences marked improvement or complete clearance, as compared to 40 percent in the placebo group. Importantly, 33 percent of patients in the calcitriol group experienced no change in their condition or worsened, as compared to 60 percent in the placebo group.

More recently, researchers noted that the combination of methotrexate and calcipotriol may result in an extension of remission time before a relapse of psoriasis. This relapse occurred in 35 days in patients who didn’t receive calcipotriol and 113 days in patients who received calcipotriol. They also noted a reduction of the methotrexate dosage needed for a satisfactory response in patients treated with calcipotriol.

Conclusion

These data suggest that the addition of topical vitamin D to other modalities increases efficacy and decreases the number of treatments required of the primary modality. Therefore, topical vitamin D therapy is both an effective adjunct to other psoriasis therapies; it has also shown to be generally safe. Not only is it associated with long-term benefit, but the combination effect seems to occur early in treatment. Given the amount of encouraging data, studies examining the effects of vitamin D with biologic therapy may be warranted, as well as greater overall inquiry into the additive benefits of vitamin D in psoriasis therapy.

More recently calcitriol (a,25-dihydroxy vitamin D3) ointment (Vectical, Galderma), a non-steroidal and biologically active vitamin D derivative, has stirred greater interest in vitamin D. It has been shown to provide significant benefit in some patients, and will likely feature prominently in the future of psoriasis therapy and research.

Dr. Bagel is on the speakers bureau for Abbott Labs, Genentech, Astellas, Amgen, Stiefel, and Warner-Chilcott.

5. Lebwohl et al. J AAD 1997: 93-95