Acitretin Plus UVB Phototherapy in the Treatment of Psoriasis

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Acitretin frequently is used in conjunction with UVB phototherapy. Home-based phototherapy is an important therapeutic option that offers greater convenience to patients. We conducted a review of the literature on acitretin and home-based phototherapy in the treatment of psoriasis with a focus on the reported efficacy, safety, cost, and practical use considerations associated with combination therapy. Acitretin plus UVB phototherapy is more efficacious than either treatment alone. Adverse events reported were similar between office-based and home-based phototherapy treatments. Acitretin is not appropriate for women of childbearing potential. Patients generally are more satisfied with home-based phototherapy than office-based phototherapy. Dermatologists should consider acitretin plus home-based phototherapy as a first-line treatment option for appropriately selected patients with psoriasis.

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Ultraviolet phototherapy is a first-line treatment option for extensive psoriasis often used in conjunction with the systemic retinoid acitretin. Either broadband (BB) or narrowband (NB) UVB phototherapy can be used. The standard approach for the administration of UVB phototherapy is to provide treatment in the physician's office, which is a safe and highly effective treatment.[1,2] However, office-based phototherapy can be inconvenient, costly, and burdensome. Home-based phototherapy is convenient and inexpensive, and is associated with both a good adherence rate and high patient satisfaction.[3]

Acitretin frequently is used in combination with either systemic medications or phototherapy.[4] The combination of acitretin plus UVB phototherapy is more effective than either therapy alone. This article reviews the use of acitretin in conjunction with home-based UVB phototherapy in the treatment of psoriasis.

METHODS

A review of the literature on combination therapy with acitretin and home-based UVB phototherapy for the treatment of psoriasis was conducted using MEDLINE/PubMed. The following search terms were employed: *combination*

therapy, phototherapy, home phototherapy, acitretin, and *psoriasis*. The efficacy, safety, cost, and practical use considerations associated with combination therapy involving acitretin and home-based UVB phototherapy were investigated.

CLINICAL DATA

Acitretin Plus Standard Office-Based Phototherapy

Acitretin administered as a monotherapy in doses of 50 mg daily is moderately effective in the treatment of psoriasis, but is associated with substantial dose-related adverse effects, including hair loss, abnormal nail formation, pyogenic granulomas, and dyslipidemia.[5] When used alone, standard phototherapy entails 2 to 3 sessions per week for a period of 12 weeks to achieve therapeutic results. Acute adverse events related to phototherapy include erythema, blistering, and dryness of the skin. Additionally, total cumulative UVB dose-related effects include photocarcinogenesis and photoaging of the skin.[1] However, it should be noted that unlike psoralen plus UVA, evidence for increased incidence of skin cancers with UVB phototherapy is lacking.[6-8] Combination therapy with acitretin plus UVB phototherapy offers multiple advantages over the use of either modality as a sole intervention in the treatment of psoriasis. Acitretin enhances the potency of phototherapy, thereby reducing the necessary dose of UV light and the treatment time for clearing of psoriatic lesions.[9] The reduction in total cumulative UVB dose associated with combination therapy reduces the risk of late-appearing adverse events, including photocarcinogenesis and photoaging.[10] Conversely, the use of phototherapy appears to confer a retinoid dose-sparing effect, thus potentially diminishing the side effects and improving tolerability of treatment with acitretin.[11]

Combination therapy with acitretin plus UVB phototherapy results in greater and more rapid improvement in psoriatic lesions. In a 12-week, placebo-controlled, clinical trial participants undergoing combination therapy (acitretin 50 mg/d plus UVB phototherapy) achieved 75% improvement in their Psoriasis Area Severity Index (PASI) scores compared to 35% improvement in participants treated with only UVB phototherapy and 42% improvement in participants who received acitretin monotherapy.[10] Another clinical trial of combination therapy with low-dose acitretin (0.34–0.44 mg/kg daily) plus UVB phototherapy in 41 participants with plaque-type psoriasis demonstrated disease clearance in 89% (8/9) of participants treated with combination therapy, 62.5% (20/32) of participants treated with UVB phototherapy, and 23% (2/9) of participants treated with acitretin monotherapy.[12] Additionally, participants who received combination therapy required a lower dose of UVB phototherapy and fewer treatments with UVB phototherapy to achieve clearance, which lead to a reduction in total cumulative UVB dose of approximately 20%.[12] Combination acitretin plus UVB phototherapy is effective in the treatment of psoriasis that is refractory to either standard phototherapy or acitretin as the sole treatment modality.[1]

Acitretin Plus Home-Based Phototherapy

Compared to standard office-based outpatient phototherapy, home-based phototherapy has similar efficacy as assessed by reduction in PASI and self-administered PASI scores, proportion of participants reaching PASI 50 and self-administered PASI 50 scores, and increase in quality of life and safety as assessed by acute adverse events and total cumulative UV dose.[13] There have been few studies to assess the efficacy of combination therapy using acitretin and home-based phototherapy (Table 1).[14-16] The combination of home-based NB-UVB phototherapy (3 sessions/wk with increased exposure time based on Fitzpatrick skin type and response to treatment) and low-dose acitretin (25 mg/d with dose adjustment as needed) in participants with moderate to severe plaque psoriasis demonstrated reduction in PASI scores with overall mean improvement in PASI scores of 22%, attainment of PASI 50 in 4 participants, and a PASI 75 in 0 participants by week 12 (N=27).[14] Additional outcomes included increased quality of life as measured by the Dermatology Life Quality Index and high satisfaction with treatment. The true efficacy of this combination might be higher, as the study duration was short and a plateau PASI improvement was not reached during the 12-week period. Furthermore, participants in this particular study stood 12 inches away from the UV lamps instead of the recommended 6 inches, thereby receiving only a fraction of the standard UV dose. Measured adherence to combination acitretin and home-based NB-UVB phototherapy in participants with moderate to severe psoriasis demonstrated good adherence to home-based phototherapy with the average number of sessions constant at 2 to 3 sessions per week while adherence to oral acitretin decreased steadily. Side effects were well tolerated and did not affect adherence to either treatment modality.[15] A recent study of low-dose acitretin (25 mg/d) in conjunction with commercial tanning bed therapy (4–5 sessions/wk) in the treatment of chronic plaque-type psoriasis demonstrated good efficacy.[16] In the retrospective study, clearance or near clearance was achieved in 83%, moderate improvement in 9%, and no improvement in 9% of participants (n=23). Additionally, participants reported

Table 1

Clinical Trials Involving Combination Therapy With Acitretin and Home-Based Phototherapy

Participants	Methods	Results	Limitations
Participants with moderate to severe plaque-type psoriasis (N=27)[14]	Following a 4-wk washout period for systemic therapies, treatment with acitretin (25 mg/d with dose modification as needed) and home-based NB-UVB phototherapy (flat-panel Pansol II unit) 3 times/wk with increasing exposure time based on Fitzpatrick skin type and response to treatment) was carried out over a 12-wk period. The use of stable topical treatments and emollients was permitted.	PASI score at week 12 was 13.9, a decrease from baseline of 18.6, constituting a 22% reduction. Four participants achieved PASI 50, and 0 reached PASI 75 by the end of the study. Mean DLQI improved from 11.9 to 7.0 over the 12-wk interval and satisfaction with treatment was high. Adverse effects: In general, the treatment was well tolerated, with mild alopecia and increased photosensitivity in a few participants. Elevated triglyceride levels were observed in several participants, necessitating a decrease in acitretin dose to 10 mg daily in 4 participants.	Small study population, short treatment duration, conservative UVB dose (12-in vs 6-in distance), and escalation of exposure time. Plateau PASI was not achieved by the end of the study, suggesting that ultimate efficacy may be higher.
Participants with moderate to severe psoriasis (N=27)[15]	Adherence to combination therapy with acitretin (10–25 mg/d) and home-based NB-UVB phototherapy (3 times/wk) for 12 wk was assessed.	Mean adherence to acitretin decreased steadily from 93.6% initially to 54.4% at wk 12 (slope, −0.24 uses/wk), with average adherence ranging from 2.5 to 7 uses/wk among study participants (n=22). Mean adherence to home-based phototherapy was steady at 2 to 3 uses/wk, with a decrease from 2.4 uses/wk initially to 2.1 uses/wk at week 12. Average adherence ranged from 0.17 to 3.5 uses/wk among study participants (n=16). Adverse effects: No significant phototoxic episodes were reported in any of the participants.	Small study population, loss of follow-up, and short duration of study.
Participants with moderate to severe plaque-type psoriasis (N=26 in the retrospective study; N=17 in the prospective trial)[16]	For the retrospective study, medical record review and participant surveys regarding compliance, satisfaction, and global assessment of improvement were conducted. For the prospective trial, combination therapy with acitretin (25 mg/d) and commercial tanning bed exposure (mean UVB output of 4.7% 4 to 5 times/wk) was carried out over a 12-wk interval.	In the retrospective study, 83% experienced clearance or near clearance, 9% had moderate improvement, and 9% had no improvement (n=23). Satisfaction with treatment was high. In the prospective trial, PASI and National Psoriasis Foundation scores demonstrated an average reduction of 78.6% and 79%, respectively. PASI 50 and PASI 75 were achieved by 76% and 59%, respectively. Adverse events were mild to moderate.	The prospective trial was limited by lack of controls and blinding and small study population.

Abbreviations: NB, narrowband; PASI, Psoriasis Area and Severity Index; DLQI, Dermatology Life Quality Index.

high satisfaction with combination acitretin and tanning bed therapy. In the prospective trial, PASI 50 and PASI 75 were achieved in 76% (13/17) and 59% (10/17) participants, respectively, and there were average reductions of 78.6% in PASI and 79% in National Psoriasis Foundation scores compared with baseline scores following 12 weeks of combination therapy. Treatment was generally well tolerated and adverse events were mild to moderate.[16]

COST CONSIDERATIONS

There is wide variability in the cost of and response to treatment in patients with psoriasis and additional costs may result from treatment failures.[17] The cost of acitretin monotherapy in 2004 was estimated at $400 per month.[18] The concomitant use of phototherapy, which confers a retinoid dose-sparing effect, may help lower the cost of long-term treatment for patients treated with acitretin. It also may help reduce costs associated with treatment failures by improving cases of psoriasis resistant to either treatment modality as the sole intervention. Conversely, low-dose acitretin increases the potency of phototherapy, thereby reducing the number of treatments required for clearing.[10] Fewer phototherapy sessions are required, thus reducing treatment time and number of phototherapy treatment sessions.[9] This may lead to better patient satisfaction and more efficient utilization of healthcare resources. The use of home-based phototherapy requires the purchase of a unit, which has associated initial and maintenance costs. However, home-based phototherapy remains the most cost-effective option compared with alternatives (including methotrexate, biologic agents, acitretin monotherapy, and psoralen plus UVA) for the treatment of patients with psoriasis.[3] From the viewpoint of insurers, a 3-month trial of home-based phototherapy can yield annual savings ranging from $2110 to $21,610 per patient compared with standard office-based outpatient phototherapy, treatment with biologic agents, or both.[19]

PRACTICAL USE CONSIDERATIONS

Timing Initiation of Acitretin Therapy

For combination therapy with acitretin plus UVB phototherapy, low-dose acitretin (usual dose, 25 mg/d) typically is administered as a single agent 1 to 2 weeks prior to the initiation of UVB phototherapy treatment. This schedule allows for minimal erythema dose (MED) testing while the patient is on a stable dose of acitretin, which frequently reduces the MED required to achieve the desired effect. UVB phototherapy treatments are then added to the regimen and this combination is continued for at least 4 more weeks.[20] For patients who are treated with NB-UVB phototherapy in conjunction with oral acitretin, the initial NB-UVB phototherapy dose is 50% of the MED. For combination regimens that involve oral acitretin and BB-UVB phototherapy, the initial BB-UVB phototherapy dose is calculated according to Fitzpatrick skin type (Table 2). The dose of acitretin is adjusted according to clinical response, which usually involves a dose reduction during the first 2 months of treatment.[22] For patients who are initiated on combination therapy who have already undergone induction of UVB phototherapy treatment, the UVB phototherapy dose should be reduced by 50% prior to the initiation of acitretin.

Dose Adjustments

Because combination therapy results in a retinoid dose-sparing effect, doses of acitretin used are usually 10 to 25 mg daily. Due to thinning of the stratum corneum associated with acitretin use, UVB phototherapy doses should be reduced by 50% to avoid phototoxicity and dosimetry should be increased gradually with additional increments of 50% of the usual amount.[20]

Laboratory Monitoring

Baseline laboratory tests, including complete blood cell count, fasting lipid panel, and liver function tests should be performed on all patients with psoriasis receiving combination acitretin plus UVB phototherapy. Follow-up laboratory tests are performed every month while dose adjustments are being made and continued thereafter as clinically indicated. Acitretin is not recommended for women of childbearing age who wish to become pregnant during or within 3 years following discontinuation of treatment. For women of childbearing age, 2 negative pregnancy tests prior to initiating acitretin treatment and monthly tests thereafter are required.[23]

DISCUSSION

The benefits of combination therapy with acitretin plus UVB phototherapy are numerous and include quicker and more complete resolution of psoriatic lesions with lower doses of both treatment modalities and thus lower potential for adverse effects and toxicity. Combination therapy with acitretin plus home-based phototherapy is a good option for patients with psoriasis who live a long distance from a treatment center and for those who find office-based phototherapy burdensome and inconvenient. Several UVB phototherapy device manufacturers offer full-body, single-panel, multiple-panel, and hand-held units for both office-based and

TABLE 2

Protocols for Combination Therapy With Acitretin and Home-Based UVB Phototherapy[21]

Combination	Acitretin Dosage and Timing	UVB Dosage and Timing	Treatment Modification
Low-dose acitretin plus BB-UVB phototherapy	Starting dose is 25 mg/d (may be adjusted by physician according to other factors) and is typically initiated 1 to 2 wk prior to initiation of BB-UVB phototherapy treatments.	Initial BB-UVB dose is determined based on Fitzpatrick skin type: (type 1, 20 mJ/cm^2; type II, 25 mJ/cm^2; type III, 30 mJ/cm^2; type IV, 40 mJ/cm^2; type V, 50 mJ/cm^2; type VI, 60 mJ/cm^2).	Acitretin: Dose of acitretin is adjusted according to clinical response. Decrease in dose of acitretin often occurs during the first 2 mo of treatment.
		The frequency of BB-UVB phototherapy treatments in association with low-dose acitretin for psoriasis is typically 3 to 5 times/wk.	Broadband-UVB phototherapy: BB-UVB dose is adjusted according to clinical response (redness, light pink color, tenderness), and dose escalation is typically 50% of the regular amount.
		If low-dose acitretin is initiated after induction of BB-UVB phototherapy treatment, dose of BB-UVB should be reduced by 50% and should not be increased for at least 2 wk.	
Low-dose acitretin plus NB-UVB phototherapy	Starting dose is 25 mg/d (may be adjusted by physician according to other factors) and is typically begun 1 to 2 wk prior to the initiation of NB-UVB phototherapy treatments.	After 1 to 2 wk of acitretin therapy, perform MED testing in the lower lumbar or sacral area. The initial dose of NB-UVB will be 50% of the MED.	Acitretin: Dose of acitretin is adjusted according to clinical response. Decrease in dose of acitretin often occurs during the first 2 mo of treatment.
		The frequency of NB-UVB phototherapy using MED treatments for psoriasis is typically 3 times/wk.	Narrowband-UVB phototherapy: NB-UVB dose is adjusted according to clinical response (redness, light pink color, tenderness), and dose escalation is calculated according to treatment number (for treatments 1–20, increase by 10% of, MED; for treatments 21 and over, dose escalation is determined by physician).
		If acitretin is initiated after induction of NB-UVB phototherapy treatment, dose of NB-UVB should be reduced by 50% and should not be increased for at least 2 wk.	

Abbreviations: BB, broadband; NB, narrowband; MED, minimal erythema dose.

TABLE 3

Phototherapy Equipment Manufacturers[a]

Company	Equipment	Web Site	Phone
National Biological Corporation 23700 Mercantile Road Beachwood, OH 44122	Full-body, hand-held, and localized BB-UVB and NB-UVB units	www.natbiocorp.com	800-338-5045
Daavlin 205 West Bement Street PO Box 626 Bryan, OH 43506	Full-body hand/foot/scalp BB-UVB and NB-UVB units	www.daavlin.com	800-322-8546
UVBioTek PO Box 430 3 Depot Street Hudson Falls, NY 12839	Full-body, wrap-around, and single-panel systems plus hand/foot units with BB-UVB and NB-UVB	www.uvbiotek.com	800-822-4683

Abbreviations: BB, broadband; NB, narrowband.

[a]Table 3 lists several manufacturers of home-based phototherapy devices for sale in the United States, which can be found on the National Psoriasis Foundation Web site.[24] Table 3 represents a sample of phototherapy device manufacturers and is not comprehensive.

home-based use (Table 3). It also is an attractive option for patients with concomitant infections or reduced immune system functioning, for whom therapy with immunomodulators (biologics and methotrexate) may be contraindicated.

Adherence to treatment remains a problem in the successful management of patients with psoriasis. Combination treatment with acitretin plus UVB phototherapy produces better results, thus increasing patient satisfaction, decreasing burden of disease, and fostering better adherence to treatment. Although an absolute increase in skin cancer risk has not been demonstrated,[6,7] the theoretical increased risk weighs heavily in the minds of some patients and physicians. The use of retinoids in conjunction with phototherapy may protect against this theoretical carcinogenicity by reducing total cumulative UV dose, exerting tumor-suppressive effects, and reversing skin cancer through the differentiation of atypical keratinocytes.[21,24] The use of combination therapy with acitretin and home-based phototherapy should be encouraged as a first-line treatment for patients with extensive psoriasis.

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