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Combination 830-nm and 633-nm Light-Emitting Diode Phototherapy Shows Promise in the Treatment of Recalcitrant Psoriasis: Preliminary Findings

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Abstract

Background and Objectives: Psoriasis is one of the major problems facing dermatologists worldwide. Planar arrays of light-emitting diodes (LEDs) have recently attracted attention in the treatment of difficult dermatological entities, 830 nm in near infrared (near-IR) and 633 nm in visible red. This study was designed to assess the efficacy of combination 830-nm and 633-nm LED phototherapy in the treatment of recalcitrant psoriasis. ***Subjects and Methods:*** Nine informed and consenting patients with psoriasis were enrolled in this preliminary study, (3 men, 6 women, mean age 34.3, skin types I to IV). All had chronic psoriasis, which in most cases had proved resistant to conventional treatments. They were treated sequentially with LED arrays delivering continuous-wave 830 nm (near-IR) and 633 nm (red) in two 20-min sessions over 4 or 5 weeks, with 48 h between sessions (830 nm, 60 J/cm^2; 633 nm, 126 J/cm^2). ***Results:*** All patients completed their LED regimens (4 requiring 1 regimen, 5 requiring a second). Follow-up periods were from 3 to 8 months, except in two patients who were lost to follow-up. Clearance rates at the end of the follow-up period ranged from 60% to 100%. Satisfaction was universally very high. ***Conclusions:*** The antiinflammatory effects of LED energy at 830 nm and 633 nm have been well documented, as has their use in wound healing. LED phototherapy is easy to apply, pain free and side-effect free, and is well tolerated by patients of all skin types. The promising results of this preliminary study warrant a proper controlled double-blind study with a larger patient population.

Introduction

One of the major problem diseases facing dermatologists in clinical practice is psoriasis, affecting between 2% and 3% of the population worldwide, despite advances in the understanding of its etiology and development of new treatment approaches. Psoriasis (from the Greek *psora* meaning 'to itch') has been recognized from biblical times and was even at one time confused with leprosy (Greek *lepra*, scaly skin, + *psora*). Although there are several phenotypes, plaque psoriasis or psoriasis vulgaris accounts for approximately 90% of cases. Psoriasis was originally believed to be a disorder primarily associated with epidermal keratinocytes leading to the typical inflammation and itchy hyperkeratotic plaques, but recent research has added an immunological component to the equation, with CD4 + T-cells that have turned "rogue," attacking instead of defending normal skin.[1,2] Various triggers have been identified, including stress, skin injury, and some streptococcal infections, and activation of the epidermal dendritic Langerhans cell, an antigen-presenting cell, by an as-yet-unknown antigen, is believed to play a major role in the psoriatic process.

Phototherapy has played a historical role in the treatment of psoriasis; exposure to sunlight, in small quantities to prevent sunburn, is known to improve psoriasis. The photosensitizer psoralen plus ultraviolet A light (PUVA) was popular a decade and more ago and is being used even now, although long-term follow-up has elicited extremely undesirable side effects such as the appearance of cutaneous melanomas.[3] The excimer laser has also been used with some success, although the areas treated are small, so large plaques take a long time to treat, and the same potential exists for UV-related carcinogenic side effects. Various pharmacotherapeutic topical and oral systemic treatments have been used, but the potential for side effects with long-term use, such as steroid-mediated skin atrophy and liver damage, is

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high. However, if treated incorrectly or left untreated, the appearance of psoriatic comorbidities has been noted, such as loss of quality of life leading to onset of depressive illness, psoriatic arthritis, and even cardiovascular disease.[4]

Phototherapy with non-UV light sources might prove interesting. The wavelength of 633 nm in the visible red waveband has been associated with good results in the treatment of acne vulgaris, another disease with a T-cell-mediated immune component,[5,6] and 830 nm in the near-infrared (near-IR) waveband has strong antiinflammatory effects;[7,8] 830 nm has also been shown to induce the production of peripheral endogenous opioids,[9] thereby potentially relieving itching. A new generation of planar-mounted light-emitting diodes (LEDs) has attracted attention in a wide spectrum of specialities, and one such system offers arrays delivering continuous light at 830 nm and 633 nm. The present preliminary study was designed to assess the effect of the combination of 830 nm and 633 nm LED phototherapy, applied sequentially, in the treatment of cases of chronic psoriasis that were recalcitrant to conventional therapies.

Subjects and Methods

Subjects

The subjects in the study included nine psoriasis patients who attended the author's institute for the treatment of their psoriasis. Eight cases had plaque psoriasis, and there was one case of guttate psoriasis. There were three men and six women, with a mean age of 34.3 ± 11.2 (range 22–58) and skin types from I to IV. All had psoriasis (body surface area involvement range 5–80%, 4 months to 35 years duration) that had proved resistant to conventional treatments. Patient demographics, history of psoriasis, and details of previous treatment regimens are seen in Table 1. All patients, having had the purpose of the study explained to them, signed consent forms to participate in the study and for clinical photography. The Ethics Committee of the Ablon Skin Institute approved the study, which was conducted under the precepts of the Declaration of Helsinki (Rev 5, 2000). None of the subjects had any history of reactivity to visible or near-IR light, and at the time of the study, none was using any kind of potentially photosensitizing medication.

System and treatment regimen

The system used was the Omnilux from Photo Therapeutics (Carlsbad, CA) fitted with the plus and revive heads, delivering 830 nm (near-IR) and 633 nm (visible red), respectively, in a continuous wave. The head used was attached to the base, and the articulated panels that make up the head were arranged to follow as closely as possible the contour of the area being treated and positioned approximately 5 cm from the skin. Each single LED session lasted 20 min, giving incident radiant fluences of $60\,J/cm^2$ for the 830-nm head and $126\,J/cm^2$ for the 633-nm head. The standard treatment regimen lasted for 5 weeks with 10 treatment sessions made up as follows: near-IR head on the first day followed 48 h later by another near-IR treatment in week 1; visible red head on the first day followed 48 h later by another visible red treatment in week 2; and near-IR treatment followed by visible red treatment 48 h later each week in weeks, 3, 4, and 5. If 100% resolution was achieved before the full 5-week regimen, LED phototherapy was stopped. If

Table 1. Patient Demographics, Psoriasis History, and Prior Treatment

Patient number	*Sex*	*Age*	*Skin type*	*Psoriasis history*	*Prior treatment*
1	M	58	II	35 years, 60% BSA (back and torso, upper and lower extremities, and groin), recent onset of psoriatic arthritis	PUVA, methotrexate, acitretin, alefacept, topical treatments (steroids, vitamin D, tazarotene gel. Moderate improvement (50% BSA) but with unacceptable side effects
2	F	34	I	14 years, 80% BSA	Methotrexate (failed), topical treatments (poor response)
3	F	29	IV	Recent onset, 30% BSA	Topical treatments, calcipotriene cream(minimal effect)
4	M	44	IV	1 years, 15% BSA (scalp, elbows, knees, posterior neck)	Olux, tazarotene gel
5	F	26	IV	3 years, 5% BSA (elbows, knees)	Ultraviolet B (no tar, failed), currently taking fluocinonide (with steroid atrophy around plaques)
6	F	37	I/II	5 years, 50% BSA, guttate psoriasis	Cephalexin, calcipotriene and betamethasone dipropionate (3 weeks), clearance except shins
7	F	22	I/II	4 months, 60% BSA (back, buttocks, elbows, knees & scalp)	Topical treatments, but no result
8	F	25	IV	1 year, 15 BSA (back, elbows)	Calcipotriene and betamethasone dipropionate for 5 months, minimal improvement
9	M	34	II/III	6 years, 40% BSA (elbows, knees, shins, buttocks, back)	Topical fluocinonide, PUVA, but poor results

BSA, body surface area; PUVA, psoralen plus ultraviolet A phototherapy.

patients were already participating in a topical regimen and the topical was not a photosensitizer, in most cases the dosage was reduced during LED phototherapy. If clearance was insufficient, or if the patient requested it, a second regimen was indicated, with the same treatment protocol as the first regimen. Patients were asked to return for regular follow-up sessions up to a maximum of 8 months. For typical home-applied adjunctive care, patients were recommended to use nonprescription over-the-counter hydrophilic ointments or oils daily to keep the plaques moist.

Results

All nine patients completed their respective treatment protocols. No adverse side effects were noted, and patients felt no pain during the treatment. Five required two regimens, and the remaining four needed only one regimen. Two patients (Patients 1 & 2) required the full 5-week, 10-treatment regimen; the others had 4 weeks with eight treatments. Resolution rates ranged from 60% to 100% (mean $91.7 \pm 13.7\%$), and follow-up periods ranged from 3 to 8

Table 2. Details of Light-Emitting Diode (LED) Treatments Per Session, Per Regimen, and Results with Follow-Up

Patient number	*LED treatment per single regimen* (regimens required, n)*	*Clearance and post-treatment follow-up*
1	Wk 1: 2×830 nm; Wk 2: 2×633 nm; Wk 3, 4, 5: 1×830 nm & 1×633 nm (2)	1st regimen: 50% (thighs), 90% (back), 80% recurrence seen 11 months post-treatment 2nd regimen: 60% (thighs), 100% (back), no recurrence in 3 months + topical treatments
2	Test treatment on large plaque right anterior shin Wk 1: 2×830 nm; Wk 2: 2×633 nm; Wk 3, 4, 5: 1×830 nm 1×633 nm (1)	100% clearance, maintained with calcipotriene and betamethasone dipropionate & tazarotene gel for 8 months. No further LED treatment required
3	Test treatment on largest plaques on elbows & knees Wk 1: 2×830 nm; Wk 2: 2×633 nm; Wk 3, 4: 1×830 nm & 1×633 nm (2)	1st regimen: 80% clearance, maintained without any other treatment for 2 months, when plaques recurred 2nd regimen: 100% clearance, but patient lost to follow-up after 6 weeks because moved out of state
4	Clobetasol propionate, tazarotene gel started concomitantly with LED treatment Wk 1: 2×830 nm; Wk 2: 2×633 nm; Wk 3, 4: 1×830 nm & 1×633 nm (1)	100% clearance by 4th treatment week. Completely clear 4 months post-treatment
5	Wk 1: 2×830 nm; Wk 2: 2×633 nm; Wk 3, 4: 1×830 nm & 1×633 nm (2)	1st regimen: 50% clearance with resveratrol-containing emollient cream plus tazarotene gel. Patient wanted 2nd LED treatment 2nd regimen: 100% clearance 2 weeks post-treatment, tazarotene gel discontinued during LED treatment. Completely clear at 6-month follow-up
6	Wk 1: 2×830 nm; Wk 2: 2×633 nm; Wk 3, 4: 1×830 nm & 1×633 nm (2)	1st regimen: 75% clearance, patient requested further LED treatment 2nd regimen: 3 sessions only, 1×830 nm, 1×633 nm, 1×830 nm, 48-h rest between each. No topicals used with LED treatment. 90% clearance of treated lesions, maintained < 10% BSA at 6 months post-treatment with no form of medication
7	Recommended to have LED treatment by friend; only back and buttocks treated with LED Wk 1: 2×830 nm; Wk 2: 2×633 nm; Wk 3, 4: 1×830 nm & 1×633 nm (2)	1st regimen: plus calcipotriene and betamethasone dipropionate and tazarotene gel, 50% clearance Patient requested further LED treatment regimen 2nd regimen: 90% clearance after 3rd week; 95% resolution after final week on back and buttocks, maintained at 80% 6 months after final treatment with topicals. Other areas treated only with topical treatments remain at 40% improvement
8	Wk 1: 2×830 nm; Wk 2: 2×633 nm; Wk 3, 4: 1×830 nm & 1×633 nm (1)	Reduced calcipotriene and betamethasone dipropionate dose, added tazarotene gel. After 2nd week, 60% clearance, improved to 90% 3 weeks post-treatment. At 3-month follow-up, 95% resolution maintained with topical calcipotriene and betamethasone dipropionate in a.m. only
9	Wk 1: 2×830 nm; Wk 2: 2×633 nm; Wk 3, 4: 1×830 nm & 1×633 nm (1)	Calcipotriene and betamethasone dipropionate started with start of LED treatment. 2 weeks post-treatment, 60% resolution. Patient did not return; lost to follow-up

*Unless otherwise stated, 48-h rest period between weekly LED sessions and second LED regimen same as first regimen.

months, except in two patients who were lost to follow-up at 2 (Patient 9) and 6 weeks (Patient 3). Patient 9 (60% clearance) failed to turn up for any further follow-up sessions. Patient 3 (100% resolution) moved to the other side of the country but was extremely satisfied with the results. In all patients with the longer follow-up periods, satisfaction rates were universally high. Details of treatment regimens, clearance rates, pharmacotherapy, and follow-up periods are shown in Table 2.

Figures 1 and 2 are typical examples of back and groin psoriasis (Patient 1), and Figure 3 is a typical example of a large area of plaque on the shin (Patient 2), both successfully treated with one full 5-week regimen of combination near-IR and red LED phototherapy, with 90% and 100% resolution maintained at 8 weeks, respectively.

Discussion

There were some limitations to this study, the first being the small patient population, which does not enable any statistical analysis of the results. However, this was only a preliminary study, and the results merit the design of a controlled, double-blinded study with an appropriately large population. Furthermore, in the present study, some patients acted as their own controls, because only some areas of their psoriasis were treated, with the untreated areas as controls. Psoriasis area and severity index scores were not applied in the present study. They are usually used in cases of psoriasis with large body surface areas, and mostly small areas were treated in this preliminary trial. A truncated form of the physician global assessment was used instead, because it can be applied equally to smaller and larger lesions.[10]

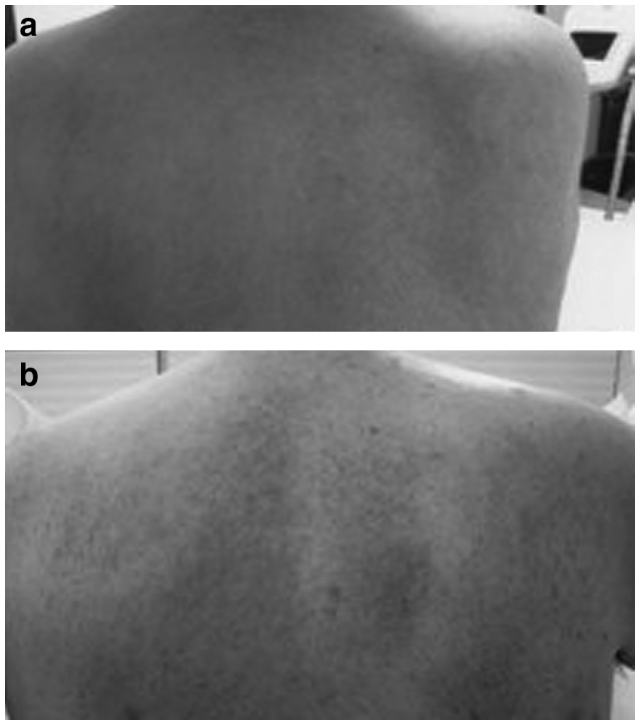

FIG. 1. Representative psoriatic plaques on the back of a 58-year-old Caucasian man (**a**) before and (**b**) 7 months after combination 830-nm and 633-nm light-emitting diode (LED) phototherapy.

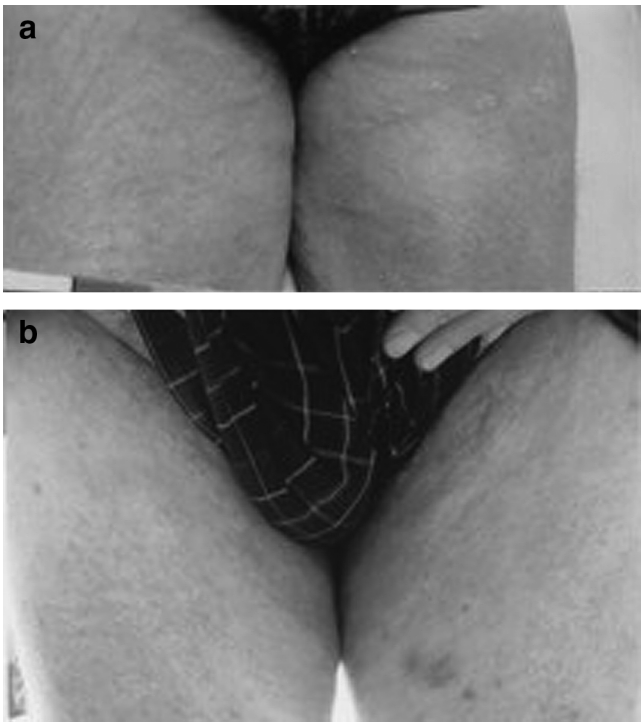

FIG. 2. Representative psoriatic plaques on the groin of a 58-year-old Caucasian man (**a**) before and (**b**) 7 months after combination 830-nm and 633-nm LED phototherapy.

The onset of psoriasis is believed to occur as follows, in a simplified version of the process.[11] An as-yet-unknown antigen activates epidermal Langerhans' cells, which then function as mature antigen-presenting cells and descend into the upper dermis, where they present the antigen to naïve CD4 + T-leukocytes, and even before the appearance of any abnormal skin pathology, clusters of these T-cells can be seen

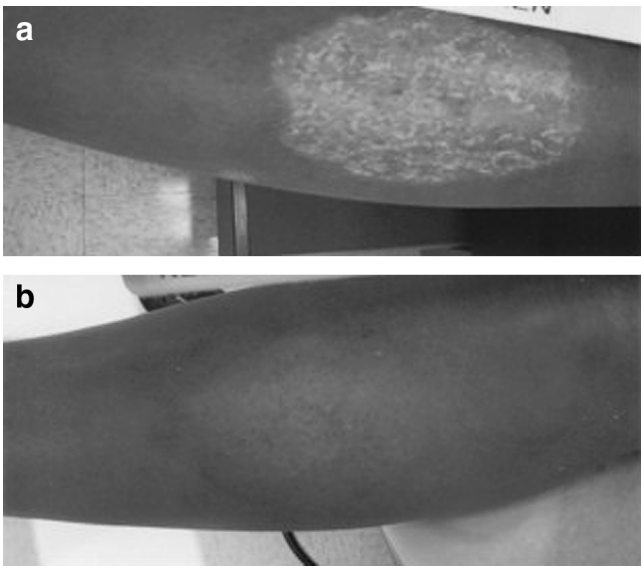

FIG. 3. Representative large psoriatic plaque on the shin of a 34-year-old Caucasian woman (**a**) before and (**b**) 8 months after combination 830-nm and 633-nm LED phototherapy.

around Langerhans' cells. The activated T-cells then migrate up into the epidermis and stimulate the basal-layer mother keratinocytes to produce a variety of proinflammatory cytokines such as interleukins, some of which are powerful keratinocytic mitogens, transforming growth factor alpha, tumor necrosis factor alpha (TNFα), and interferons, all of which descend into the dermis and further upregulate the inflammatory process. While this has been happening, the chemotactic signaling released in the dermis by the activated CD4 + T-cells has recruited neutrophils through the capillaries through the production of intracellular adhesion molecule 1, endothelial adhesion molecule 1, and recruitment of mast cells, which add to the inflammation by degranulating.

Even more activated T-cells head up into the epidermis and further stimulate keratinocyte activity and the release of more cytokines into the basal layer and dermis. This enhances the overproduction of upwardly moving daughter keratinocytes, which make up the stratum spinosum and eventually degrade into the keratin flakes of the stratum corneum. The normal skin cell cycle of approximately 28 days is compressed into 2 to 6 days, and there is a log-jam of daughter keratinocytes and a rapidly proliferating stratum corneum, plus the inflammation caused by the proinflammatory cytokines helped on by T-cells which have turned "rogue," attacking normal skin cells instead of protecting them. Thus, psoriasis represents an immune-regulated vicious circle, which is formed and maintained based on the constant movement of T-cells to and from the epidermis, constant overproduction of keratin from the activated keratinocytes, and the boosted dermal inflammatory process. The overproduction of keratin flakes also disrupts the integrity of the stratum corneum and ceases to act as a protective boundary against environmental inflammatory agents, adding to the overall inflammation.

The most obvious approach would be to identify the original causative antigen that the Langerhans' cells deliver to the dermal CD4 + T-cells, and this is being actively investigated but without any success to date, although it is believed to be associated with streptococcal infection.[2] The next avenue of attack would be to deactivate the rogue T-cells before they can start to upregulate the mother keratinocyte activity, and research is currently focusing on probiotics that could accomplish this. Whatever approach is taken, it should seek to break the vicious circle between the T-cells, the hyperactive keratinocytes, and the abnormally accelerated inflammatory response and relieve the severe itching, while at the same time helping to repair the dermal and epidermal morphological disruption caused by the process of the disease.

The near-IR wavelength of 830 nm has been shown to have strong antiinflammatory properties[7,8] and produces endogenous opioids, which are capable of calming the peripheral neural receptor stimulation perceived as itching.[9] In addition, 830 nm significantly enhances local blood flow rate and volume,[12] and although that might not at first appear to be helpful in an inflammatory state, it also increases concomitant lymphatic flow and drainage so that normal reparatory and defensive cells are recruited into the zone of interest in large numbers, thus helping to normalize the situation. Red light at 633 nm has been associated with treating the stress-related and hormonal factors of acne, in addition to its already proven effect on inflammation.[5,6] LED energy at 633 nm in humans *in vivo* has also been proved to recruit large numbers of Th1 and Th2 skin-homing T-cells into the irradiated skin,[13] which might help to replace the rogue T-cell population and break the vicious circle in psoriatic skin. The same combination LED therapy in a 4-week alternating regimen of 830 nm followed 24 to 72 h later by 633 nm has been convincingly and objectively shown to produce strong collagen and elastin synthesis in a large-population controlled study of skin rejuvenation.[14] This could assist in the repair process of the psoriasis lesion after the vicious circle has been broken.

Conclusion

Taking the above into consideration, it might then be possible to explain the excellent and robust effect that combination near-IR and visible red LED phototherapy had in the subjects of this preliminary study, giving 90% to 100% clearance of recalcitrant lesions in eight of the nine subjects. LED phototherapy is easy to apply, is pain free and side effect free, and is well tolerated by patients of all ages and all skin types. A future controlled, double-blind study is thus warranted in a larger patient population to confirm the excellent results of the current preliminary study.

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