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A Preliminary Study to Assess the Efficacy of a New UVA1 Laser for Treatment of Psoriasis

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Abstract

Objective: The aim of the present study was to assess the effectiveness of an UVA1 355 nm laser (Alba 355) for treatment of mild, moderate, and severe psoriasis. ***Background data:*** Psoriasis is an immune-inflammatory and proliferative skin disease. During the past few years, the instrumental treatment by UV radiation has been successfully described, either alone or in combination with topical and/or systemic drug administration to treat several skin-related diseases. ***Materials and methods:*** Fourteen patients, aged between 25 and 50 years, affected by mild-to-severe psoriatic plaques, were included in this study. Patients were treated with a new instrument, laser Alba 355, which administers energy in the UVA1 spectrum. This instrument is based on a 1064 wavelength neodymium-doped yttrium orthovanadate (Nd:YVO4) laser optically pumped using a 808 nm infrared beam able to achieve a third harmonic 355 nm wave delivery. The fluences administered were 80–140 J/cm^2 four times a week for a total of up to 12 sessions over selected psoriatic plaques in different areas of the patients' bodies. The patients rated their satisfaction with the outcome of the procedure as 1 not satisfied, 2 quite satisfied, 3 very satisfied. ***Results:*** Overall, laser treatment of psoriatic plaques produced a significant improvement in Psoriasis Area and Severity Index (PASI) score (F [3, 55] = 57.86; $p < 0.001$). The mean PASI score decreased from a baseline value of 24.5 ± 2.9 to a value of 15.6 ± 1.9 at 1 week ($p < 0.001$), 9.1 ± 1.2 at 2 weeks ($p < 0.001$), and 5.8 ± 1.2 at 3 weeks ($p < 0.001$) (all data reported as mean ± standard error of the mean). All the patients were very satisfied with the outcome of procedure. No side effects were observed in this study. ***Conclusions:*** The present study outlines an original approach based on UVA1 355 nm laser therapy for treatment of mild, moderate, and severe psoriasis. In the present study, the high success rate was coupled with safety. Larger clinical trials are needed to definitely support the role of this medical device not only for treatment of psoriasis, but also for other skin-related diseases that share a similar pathophysiology. We speculate that in the near future, the use of this laser will grow in the dermatological field.

Introduction

Psoriasis is a chronic, immune-mediated inflammatory disorder with a 2–3% incidence among the Caucasian populations in Western countries.[1] During the past few years, physical therapies of chronic dermatopathological diseases have aroused the attention of a growing number of clinicians because of their proven effectiveness, especially when joined with pharmacological and pharmacobiological treatments, inducing a fast and long-lasting improvement in patients' symptoms and quality of life. This therapy is particularly effective in the long run and when facing conditions resistant to topical treatments and chronic diseases. In order to understand the rationale of radiation therapy in dermatology, we have reported a diagram describing the radiations that can be used basing on the evidence that, within the electromagnetic spectrum, ultraviolet (UV) radiation is classified according to the wavelength measured in the UVC (200–290 J/cm^2), UVB (290–320 J/cm^2), and UVA (320–400 J/cm^2) ranges (Fig. 1); the latter can be divided in UVA2 (320–340 J/cm^2) and UVA1 (340–400 J/cm^2).[2] Among them, the UVB radiation is characterized by a wavelength between 290 and 320 nm (especially the narrow-band UVB radiation with a more efficacious spectrum ranging between 310 and 313 nm) and induces apoptosis in T-lymphocytes and immunocompetent cells that are involved in chronic inflammation and in the pathogenesis of many skin-related diseases, including psoriasis.[3–5]

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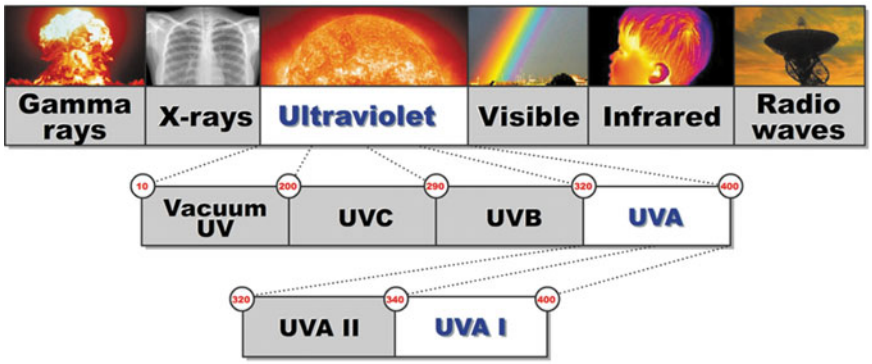

FIG. 1. Electromagnetic spectrum.

From a therapeutic perspective, UVA1 irradiation has been categorized as low (10–40 J/cm^2), medium (40–80 J/cm^2), and high (80–120 J/cm^2) dose regimens. Low doses are administered with fluorescent lamps, with low-cost instrumentation and maintenance costs. High energy fluences (>100 J/cm^2) can be delivered only with metal-halide lamps that are associated with high costs and time-limited fluorescence.[6,7]

UVA1 and UVAB radiation produce photoisomerization of *trans*-urocanic acid (UCA). Furthermore, exposure of human skin to UVA1 and UVB light results in an increase in percentage of *cis*-UCA in suction-blister fluid.[8] However, UVA1 therapy presents peculiar characteristics. For example, in contrast with UVB and psolaren UVA (PUVA) therapy, UVA1 radiation produces an immediate apoptotic rather than a delayed apoptotic state by means of constitutive intracellular proteins, instead of requiring accumulation of newly synthesized proteins such as p53.[9] Furthermore, whereas UVB light produces an increase in tumor necrosis factor-alpha (TNF-α) in suction-blister fluid in human skin, an opposite effect is observed following UVA1 therapy.[8] Interleukin (IL)-10 is also significantly increased in suction-blister fluid in human skin following UVB, but not UVA1, irradiation.[8]

UV lasers have been extensively evaluated in the field of dermatology. For example, Gomez and colleagues[10] showed that UV radiation (355 nm), emitted by a Nd:YAG laser, required a lower energy for the ablation of the stratum corneum, inducing a greater impact on the lipid structures without any risk of producing lesions to the epidermis, if compared with infrared (IR; 1064 nm) radiation. Sato and colleagues[11] evaluated UV radiation-mediated ablation (355 nm) in porcine myocardium tissue samples using 1064, 532, and 266 nm radiations, showing that the ablation depth was maximized at 355 and 1064 nm through a photo-dermal process. This study emphasised how this laser could be potentially relevant to achieve transmyocardial revascularization for treatment of ischemic heart disease.

Excimer light devices (ELD) have also been widely used for treatment of psoriasis. For example, a study using a 308 nm monochromatic excimer light, showed a complete remission in more than 50% of patients (average of 12 sessions) with psoriasis involved in this investigation (152 patients with stable and localized plaque psoriasis, 47 with palmoplantar psoriasis).[12] This evidence was also confirmed by Wollina and coworkers [13] who showed an improvement in Psoriasis Area and Severity Index (PASI) score in patients with moderate plaque-type psoriasis treated with a 307 nm ELD. This improvement was equivalent to topical dithranol twice daily, but it was achieved in a significantly shorter time. The literature, regarding the use of excimer light, has also been reviewed by Gattu and coworkers showing that 18 clinical trials report positive results concerning the use of 308 nm excimer devices in psoriasis vulgaris, scalp psoriasis, and palmoplantar psoriasis,[14] further supporting the use of this device for treatment of different types of psoriasis.

UVA1 therapy has also been used for treatment of atopic dermatitis, localized scleroderma, systemic lupus erythematosus, polymorphic light eruption, cutaneous T cell lymphoma, lichen sclerosus, keloids, systemic sclerosis, and hand dermatitis.[5]

In the context of psoriasis, UVA1 therapy has been used in combination with tacrolimus[15] and calcipotriol,[16] showing negative and positive results respectively. A study has also used UVA1 light to treat three patients affected by psoriasis of the palms, reporting no improvement in a patient and a 25–50% improvement in two subjects.[17]

Objective

The aim of the present study was to investigate the therapeutic effectiveness of UVA1 355 nm laser for treatment of mild, moderate, and severe psoriasis.

Materials and Methods

Patients

A total of 14 patients (n [men] = 10; n [women] = 4; age = 25–50 years [37.7 ± 2.3; mean ± standard error of the mean (SEM)]), affected by psoriasis, were involved in this study. Two men and a woman were classified as affected by mild psoriasis (basal PASI score = 7.4, 9.6, 8.1). A woman was classified as affected by moderate psoriasis (basal PASI score = 19.6) and eight men and two women were classified as affected by severe psoriasis (basal PASI score = 20.5, 30.7, 28.9, 22.9, 21.7, 29.1, 26.5, 43, 37.8, 38). All patients signed the informed consent to participate in this study. The study was conducted in accordance with the Declaration of Helsinki and the local Institutional Review Board (IRB). All the patients were asked to suspend previous pharmacological and physical therapies 30 days before the beginning of the study. Exclusion criteria were absence of concomitant cutaneous pathologies, such as cutaneous epithelioma and HIV-associated psoriasis. The PASI score was used to measure the severity of the psoriatic lesions following UVA1 laser therapy.[18] PASI score assessed four body regions: head, trunk, upper extremities,

and lower extremities. For each region, the surface area involved was graded from 0 to 6 and each of the three parameters, erythema, thickness, and scaling of the plaques, was graded from 0 to 4. The scores from the regions were summed to give a PASI score ranging from 0 to 72. Psoriatic patients were classified into mild (PASI < 10), moderate (PASI ≥ 10 but ≤ 20) and severe (PASI > 20), according to the working definitions of disease severity in psoriasis adapted from the European Medicines Agency (see EMEA Committee for Proprietary Medical Products. Note for guidance on clinical investigation of medical products indicated for the treatment of psoriasis. CPMP/EWP 2454/02).

Patients underwent a preliminary hematochemical screening and an evaluation of lesions from a morphologic and photographic perspective. The therapeutic protocol consisted of the administration of moderate-to-high frequencies (80–140 J/cm^2), according to the lesion phototype and morphology. Lesions were treated four times a week for up to 3 weeks (13 ± 1.21; mean ± SEM). The patients rated their satisfaction with the outcome of the procedure as 1 not satisfied, 2 quite satisfied, 3 very satisfied. Each session lasted up to 1 h and 40 min. Every lesion was treated for 25 min with the laser beam moving back and forth on top of the area that required treatment. During the therapeutic sessions, the patients were wearing protective glasses, whereas the cutis did not need any protection as psoriatic plaques were selectively treated.

Light source

The energy administered in the UVA1 spectrum was produced using a new laser technology, laser Alba 355 (Elettronica Valseriana, Casnigo, Italy) (Fig. 2, Table 1). The solid-state laser uses an active medium and a neodymium-doped yttrium orthovanadate (Nd:YVO4) crystal that is energetically pumped by another laser with 808 nm wavelength. The light emitted by the Nd:YVO4, at a wavelength equal to 1064 nm, is pulsed through an acousto-optic crystal called Q-switch, which produces a frequency of 20–50 kHz and transforms the laser light into an ultrashort pulsed light (25 ns). This pulse rate is higher than 40 kW and it is sent to crystals in order to duplicate and triplicate the 1064 nm wavelength-producing second (532 nm) and third (355 nm) harmonic wavelength delivery. The laser beam is then filtered by a harmonic separating mirror in order to select from its galvanometric head a 355 nm wavelength-specific beam that is amplified and homogenate, just before galvanometric head output, with a 2.5 mm spot and a pulse-repeating potential up to 20,000 spots/sec, thus designing variously shaped bidimensional figures. The 355 laser peak power intensity is quite high, thus achieving adequate energy fluences, such as 0.25 J/cm^2, with a galvanometric pulse reinduction of 2000 mm/sec; 100 J/cm^2 can be delivered in 20 sec.

FIG. 2. Laser Alba 355 (Elettronica Valseriana, Casnigo, Italy).

Table 1. Laser Alba 355 Technical Characteristics

Laser source	DPSS (solid state laser diode pumped)
Active material	Nd:YVO4
Wavelength	UV (355 nm)
Maximum output	7 W
Beam size	2.5 mm
Beam quality	TEM00
Beam divergence	1.5 mrad
Power stability	< 1%
Pulse repetition rate	20–25 kHz
Maximum energy per pulse	0.35 mJ
Pulse width	10–15 ns
Cooling system	Air

Statistical analysis

Statistical analyses were performed using GraphPad Prism 5 software. Data were first checked for normality using the Anderson-Darling test. A one-way ANOVA followed by Bonferroni *post-hoc* test was applied. Data are presented as mean ± SEM. A value of $p < 0.05$ was considered significant.

Results

The overall laser treatment of psoriatic plaques produced a significant improvement in the PASI score (F [3, 55] = 57.86; $p < 0.0001$) (Fig. 3). The mean PASI score decreased from a baseline value of 24.5 ± 2.9 to a value of 15.6 ± 1.9 at 1 week ($p < 0.001$), 9.1 ± 1.2 at 2 weeks ($p < 0.001$), and 5.8 ± 1.2 at 3 weeks ($p < 0.001$). A reduction of 76.7 ± 10.9% in the PASI score was observed at 3 weeks in the four patients classified as affected by mild and moderate psoriasis after 9.2 ± 0.3 sessions (Fig. 3). In the 10 patients classified as affected by severe psoriasis, a reduction of 89.4 ± 2.4% was observed

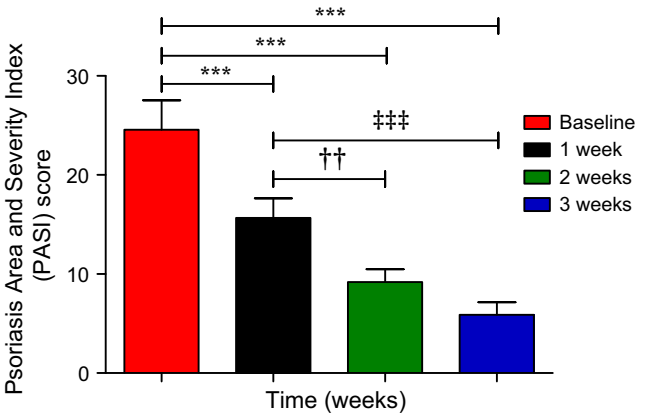

FIG. 3. Psoriasis Area and Severity Index (PASI) score at baseline and after 1, 2, and 3 weeks of treatment by means of laser Alba 355. ***$p < 0.001$ versus baseline, ††$p < 0.01$ versus 1 week, ‡‡‡$p < 0.001$ versus 1 week.

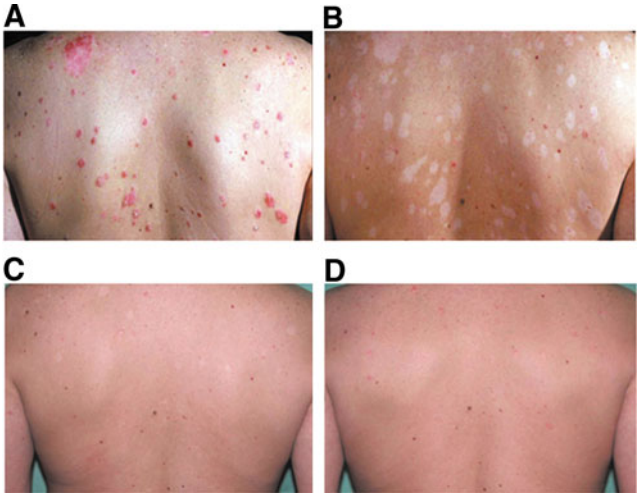

FIG. 4. Patient affected by mild psoriasis **(A,B)** before and **(C,D)** after 10 treatment sessions of laser therapy over a period of 2 weeks.

after 11.4 ± 0.2 sessions (Fig. 3). Therefore a 75% reduction in the PASI score (PASI 75), which is considered a benchmark of primary endpoints for many clinical trials of psoriasis,[19–21] was observed in 12 out of 14 patients who participated in this investigation. All the patients were very satisfied with the outcome of the procedure. No adverse reactions were observed during the study. Examples of patients affected by psoriasis before and after laser treatment are shown in Figs. 4–7.

Discussion

The present study shows an overall significant improvement in the PASI score in patients treated for up to 3 weeks with four sessions a week of UVA1 laser therapy. These patients were affected by mild, moderate, and severe psoriasis and were treated with moderate-to-high frequencies (80–140 J/cm^2). Our findings support the clinical use of a monochromatic coherent and coordinate UVA1 light laser therapy alone for treatment of this condition. These results are not in agreement with a previous study where treatment with UVA1 irradiation of three patients, affected by psoriasis of the palms, produced no improvement in a patient and only a 25–50% improvement in the other two.[17] With regard to UVA1 irradiation and pharmacological treatment, contrasting results have been previously reported. For example, a previous study of medium-dose UVA1 (50 J/cm^2) and tacrolimus ointment showed no dramatic changes in plaque thickness or scaling in five patients affected by palmar plantar psoriasis.[15] On the other hand, another study, comparing calcipotriol in combination with UVA1 to calcipotriol with narrow-band UVB phototherapy in 45 patients with plaque psoriasis, concluded that UVA1 phototherapy with calcipotriol is effective and could be an alternative to narrow-band UVB phototherapy with calcipotriol.[16]

The UVA1 355 nm laser (Alba 355) used in this study presents many advantages. First, it is cheaper if compared with metal-halide lamps that also require constant maintenance to maintain high tube brightness. Second, it is able to maintain a stable brightness for a number of hours consisting of 20,000 deliveries and with the possibility to deliver up to 100 J/cm^2 in 20 sec. This feature allows a selective treatment of 100 J/10 cm^2 psoriatic plaques in 4 min.

In the present investigation, we did not observe any side effects. However, side effects following UVA1 irradiation have been reported. Acute side effects include hyperpigmentation, redness, dryness and pruritus, herpes simplex virus reactivation, and polymorphic light eruption induction.[7] Chronic side effects include photoaging and possible photocarcinogenesis.[7] It is important to underline that previous studies reporting these complications could not confirm their association with UVA1 radiation, as the patients

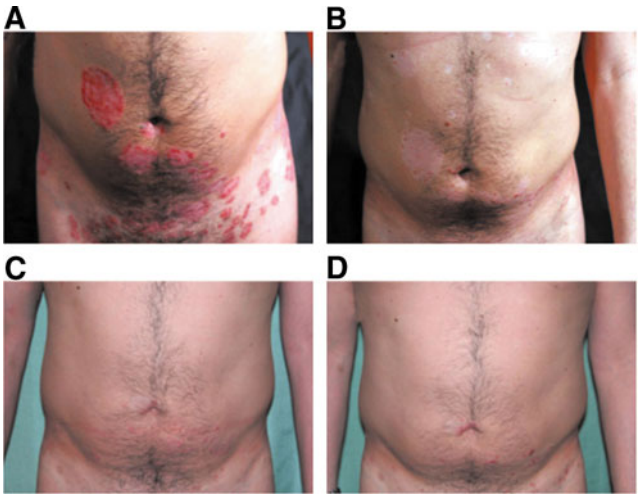

FIG. 5. Patient affected by severe psoriasis **(A,B)** before and **(C,D)** after 12 sessions of laser therapy over a period of 3 weeks.

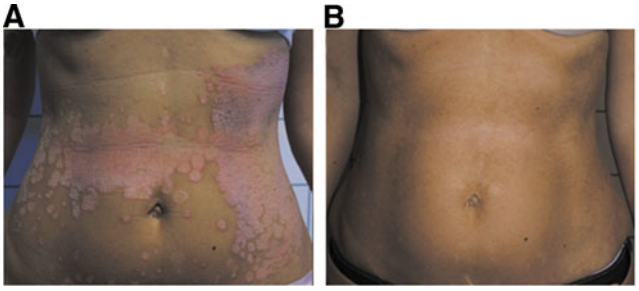

FIG. 6. Patient affected by severe psoriasis **(A)** before and **(B)** after 8 sessions of laser therapy over a period of 2 weeks.

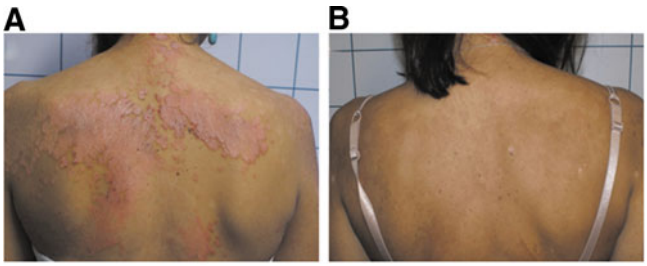

FIG. 7. Patient affected by severe psoriasis **(A)** before and **(B)** after 12 sessions of laser therapy over a period of 3 weeks.

had also received other treatments.[22,23] Furthermore, side effects associated with UVA1 radiation are fewer if compared with those from other types of phototherapy.[7]

Conclusions

In conclusion, our preliminary study of UVA1 therapy alone for treatment of mild, moderate, and severe psoriasis produced positive results in our cohort of patients. Larger clinical trials are needed to definitely support the role of this medical device not only for treatment of psoriasis, but also for other skin-related diseases. We speculate that, in the near future, the use of this laser will grow in the dermatological field.

Author Disclosure Statement

No competing financial interests exist.

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