Photodynamic Photorejuvenation

R. Ruiz-Rodriguez, MD, T. Sanz-Sánchez, MD, and S. Córdoba, MD

Department of Dermatology, Clínica Ruber, Madrid, Spain

BACKGROUND. **The visible signs of photodamage are characterized by wrinkling, coarse skin texture, pigmentation alterations, telangiectases, and in some case actinic keratosis (AKs). Intense pulsed light (IPL) photorejuvenation has been shown to improve each of the different components of photodamaged skin except AKs.**

OBJECTIVE. **To present photodynamic therapy with topical 5-aminolevulinic acid (ALA-PDT) using IPL as a light source for treatment of AK in patients having IPL photorejuvenation.**

METHODS. **Seventeen patients with varying degrees of photodamage and AKs (total of 38 AKs) were treated with two treatments with a 1-month interval of ALA-PDT using IPL as a light source.**

RESULTS. **Thirty-three of 38 AKs disappeared with two ALA-PDT treatments using IPL. The follow-up period was 3 months. The technique was very well tolerated. Erythema and crusting took 1 week to resolve in the AK area. The cosmetic results were excellent in all patients without pigmentary alterations or scarring.**

CONCLUSION. **This study describes a new application of IPL technology. Patients who are candidates for photorejuvenation procedures presenting with AKs can now have AKs treated as part of the photorejuvenation process rather than necessitating separate topical therapy with 5-fluorouracil (5-FU) or cryotherapy. In addition, many patients with AKs may benefit from the combination treatment with 5-ALA and IPL.**

R. RUIZ-RODRIGUEZ, MD, T. SANZ SÁNCHEZ, MD, AND S. CÓRDOBA, MD HAVE INDICATED NO SIGNIFICANT INTEREST WITH COMMERCIAL SUPPORTERS.

RECENTLY A flashlamp that emits noncollimated, noncoherent light, or intense pulsed light (IPL) has been shown to induce mild improvement in rhytides without epidermal ablation.[1] The emitted wavelengths can range from 550 to 1200 nm in the visible to near-infrared spectrum. A filter is used to selectively block and define wavelengths below a certain threshold.

Photodynamic therapy with topical 5-aminolevulinic acid (ALA-PDT) followed by irradiation with red light is a well-known treatment for actinic keratosis (AK), superficial basal cell carcinomas (BCCs), and Bowen disease.[2,3] The use of ALA-PDT for viral infections such as herpes simplex, molluscum contagiosum, and verrucae vulgaris has been suggested.[4]

The visible signs of photodamage are characterized by wrinkling, coarse skin texture, pigmentation alterations, telangiectases, and in some cases AK. IPL photorejuvenation is able to improve each of the different components of photodamaged skin except AKs.[5,6] In this article we show that ALA-PDT using IPL as a light source is an effective treatment for both photorejuvenation and AKs.

Address correspondence and reprint requests to: Ricardo Ruiz-Rodriguez, MD, Policlínico Ruber, C/Maldonado 50, 28006 Madrid, Spain, or e-mail: ricardo@rruiz.org.

Case Reports

Seventeen patients (13 women and 4 men) with at least one AK and chronic actinic damage were selected for photorejuvenation with IPL. All patients were of Fitzpatrick skin types II–III. A total of 38 lesions of AK on the face and scalp were valuable at 1 and 3 months after the second treatment. All the AKs had not been treated in the last 6 months. Clinically typical AKs were selected by three dermatologists as scaly erythematous papules and plaques devoid of cystic pores or a papillomatous surface (to exclude seborrheic keratosis and verrucae). Pregnant or nursing women or patients with a history of cutaneous photosensitivity were excluded.

Twenty percent 5-aminolevulinic acid (5-ALA) was mixed in an oil-in-water emulsion and was applied 4 hours prior the rejuvenation treatment in a thick layer (0.2 g/cm^2) only on the AK area in all patients. Plastic film was placed over the cream for 4 hours to increase penetration.

Treatment was performed using the Epilight device (ESC/Sharplan Medical Systems, Needham, MA), which emits flashlamp-stimulated noncoherent light filtered to limit wavelengths from 590 to 1200 nm. For the treatment of AKs we used a cutoff filter of 615 nm with a total fluence of 40 J/cm^2 with a double pulse mode of 4.0 msec and a delay time of 20 msec between pulses in a single treatment. For the rest of the face we used the parameters published by Bitter.[5] We used EMLA

ISSN: 1076-0512/02/$15.00/0 • Dermatol Surg 2002;28:742–744

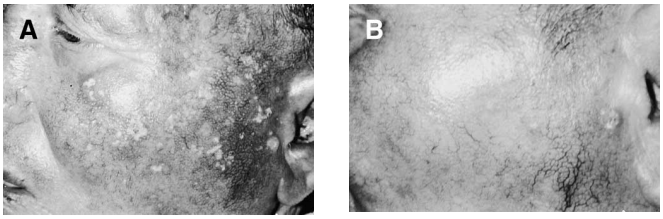

Figure 1. A) A 77-year-old man with coronary disease on anticoagulant treatment. B) One month later after one treatment.

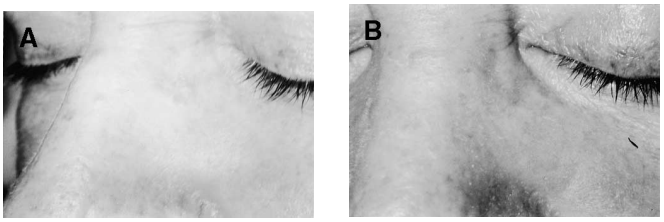

Figure 3. A) A 50-year-old women with AK on her nose (left superior area). B) One month after one treatment.

on the non-AK area of the skin 2 hours prior to the treatment.

The treatment was very well tolerated. All patients experienced mild discomfort during light treatment on the AK area. Immediately after irradiation, erythema and edema were seen in all AKs treated, with crusting followed by uncomplicated healing in 10 days. At 1 month we repeated the treatment in all patients. We performed two treatments on each patient with a 1-month interval and the follow-up visits were 1 and 3 months after the second treatment. One month after the first treatment (just prior to the second treatment) we observed the resolution of 29 of 38 AKs (76.3%). At the 1-month and 3-month follow-ups there was no visible AK in 15 of 17 patients. From a total of 38 AKs treated we observed the resolution of 33 AKs (91%), and a great improvement of the 5 resistant AKs. We observed the same results at the follow-up visits 1 and 3 months after the second treatment. The evaluation of the resolution of the AKs was made by clinical inspection by three dermatologists and by photography. We performed a punch biopsy on the scalp of a patient with AKs 3 months after the second treatment which showed no epidermal abnormalities or signs of dysplasia. The cosmetic results were excellent in all patients, without pigmentary alterations or scarring (Figures 1–4).

Discussion

The results of this study show that ALA-PDT using IPL as the light source is a highly effective, simple, and well-tolerated method for the treatment of AKs, particularly in patients having IPL rejuvenation treatments. Two treatments with a 1-month interval using topical application of 20% ALA for 4 hours on AK lesions followed by treatment with IPL for photorejuvenation resulted in complete clearing of 34 of 38 AKs in 17 patients with a 3-month follow-up period. All patients reported mild discomfort during IPL exposure on AKs but did not require local or topical anesthesia. Immediately after irradiation, erythema and edema were seen in all treated AKs, with crusting followed by uncomplicated healing in 10 days. An excellent cosmetic result was obtained, with no pigmentary alterations or scarring.

When ALA penetrates the altered stratum corneum of AKs it is absorbed in the keratinocytes and is converted enzymatically into the endogenous photosensitizer protoporphyrin IX (PpIX).[7–9] Illumination of cells containing PpIX with light of appropriate wavelength releases cytotoxic radicals. PpIX has a maximum absorption at 410, 630, and 690 nm. Most ALA-PDT studies for treatment of cutaneous lesions have used full-spectrum unfiltered visible light (400–700 nm), red noncoherent light, or red laser light to maximize the activation of the PpIX at all levels of the skin and superficial dermis in an attempt to induce the greatest response of the AK and to maximize the clinical cure rate. A new ALA-PDT system has been recently manufactured for nonhyperkeratotic AK using blue light (400–450 nm). We use a 615 nm cutoff filter to include the absorption peaks of PpIX at 630 and 690 nm and to achieve deeper penetration.

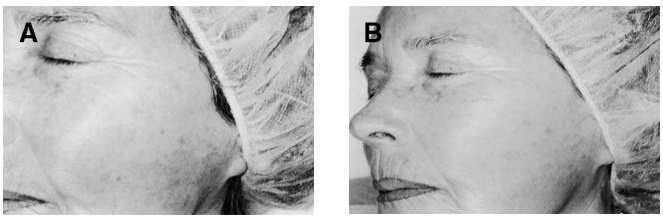

Figure 2. A) A 65-year-old woman with AK on her left cheek. B) One month after one treatment. You can see an improvement of her skin and the disappearance of the AK.

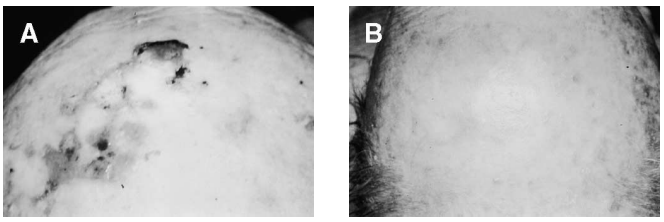

Figure 4. A) A 76-year-old man with AK (biopsy proven) on his scalp resistant to previous treatments with multiple cryotherapy and 5-FU. B) One month after one treatment.

Daily therapy with 5-FU lasts for several weeks to achieve clinical efficacy. Erythema, crusting, and discomfort may be unacceptable to some patients. Weekly "pulse" dosing has decreased the magnitude of erythema and eliminated most of the crusting, but still requires therapy for 7 weeks. ALA-PDT with IPL is similar to a peel and liquid nitrogen therapy in that it is accomplished with a single treatment and results in a 10-day healing phase, but ALA-PDT is more selective in directing maximal injury to the AKs with relative sparing of the surrounding skin, obtaining better cosmetic results. From our experience using IPL, we believe that the resolution of AKs has occurred from the combination of IPL plus topical drug and not from the IPL.

This study investigated a new and unique application of IPL in the visible improvement of AKs. We conclude that ALA-PDT using IPL as the light source is an effective, simple, well-tolerated, and safe method for treating AKs. Patients who are candidates for photorejuvenation procedures who present with AKs can now have AKs treated as part of the photorejuvenation process rather than requiring separate topical therapy with 5-FU or cryotherapy. In addition, many patients with AKs may benefit from the combination treatment with 5-ALA and IPL. Further study is necessary to determine the long-term clearance of AKs with the described technique as well as the practicality and safety of treating the entire face with this technique for resolution of incipient AKs.

References

1. Golberg DJ, Cutler KB. Nonablative treatment of rhytides with intense pulsed light. Lasers Surg Med 2000;26:196–200.
2. Fritsch C, Goerz G, Ruzicka T. Photodynamic therapy in dermatology. Arch Dermatol 1998;134:207–14.
3. Kalka K, Merk H, Mukhtar H. Photodynamic therapy in dermatology. J Am Acad Dermatol 2000;42:389–413.
4. Stender IM, Na R, Fogh H, Gluud C, Wulf HC. Photodynamic therapy with 5-aminolevulinic acid or placebo for recalcitrant foot and hand warts: randomised double-blind trial. Lancet 2000;355:963–6.
5. Bitter PH Jr. Noninvasive rejuvenation of photodamaged skin using serial, full face, intense pulsed light treatments. Dermatol Surg 2000; 26:835–43.
6. Negishi K, Tezuka Y, Kushikata N, Wakamatsu S. Photorejuvenation for Asian skin by intense pulsed light. Dermatol Surg 2001;27: 627–32.
7. Divaris DXG, Kennedy JC, Poittier RH. Phototoxic damage to sebaceous glands and hair follicles of mice after systemic administration of ALA correlates with PpIX fluorescence. Am J Pathol 1990;136: 891–7.
8. Penq Q, Berg K, Moan J, Kongshaug M, Nesland JM. 5-aminolevulinic acid-based photodynamic therapy: principles and experimental research. Photochem Photobiol 1997;65:235–51.
9. Kloek J, Akkermans W, Beijersbergen van Henegouwen GM. Derivatives of 5-aminolevulinic acid for photodynamic therapy: enzymatic conversion into protoporphyrin. Photochem Photobiol 1998;67: 150–54.

Commentary

The use of ALA with IPL as a method of photodynamic photorejuvenation is intriguing and appears to be efficacious from this report. Unfortunately there are some flaws in the basic study design that make it difficult for us to be sure of these data. The author lists inclusion criteria of at least one actinic keratosis and chronic actinic damage, as well as a Fitzpatrick skin type of II or III. I think the patients with only one or two keratoses and those with many actinic keratoses are actually two different study populations. Those with multiple actinic keratoses tend to have widespread epidermal dysplasia and a much higher recurrence after therapy. It would have been useful to divide the patients according to the extent of their photodamage.

There were no biopsies taken before the treatment, so we have no idea how severe the epidermal dysplasia is with these patients. Although 17 patients were treated, there was only one posttherapy biopsy. There is no independent observer looking at the changes in photodamage in these patients. There is no control side, using another therapy placebo to see how many of these actinic keratoses might have spontaneously resolved.

This is a good preliminary report, however, one would need to follow these patients at least 1 year and preferably 3 years because this is the time period in which recurrence has been shown to occur both with chemical peels and with Effudex. In addition, the follow-up on these patients is much too short.

We are always looking for better ways to treat widespread actinic keratoses. I would encourage the authors to do a follow-up study of this preliminary work.

NAOMI LAWRENCE, MD
Marlton, NJ