

# Treatment of Photoaging with Topical Aminolevulinic Acid and Light

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## ABSTRACT

*Photodynamic therapy (PDT) has been used for several years for the treatment of actinic keratoses and prevention of invasive nonmelanoma cancers. More recently, increasing physician expertise with the topical sensitizers and light sources employed in PDT has led to expanded applications, including its use for improvement of the visible signs of photoaging. Aesthetic treatment of photoaged skin with brief application of topical 5-aminolevulinic acid followed by well-tolerated light sources, such as intense pulsed light or pulsed-dye laser, can enhance the effectiveness of nonablative laser treatment without increasing adverse effects or downtime.*

**Key Words:** *photodynamic therapy, intense pulsed light, pulsed-dye laser, aminolevulinic acid, photoaging*

Nonablative laser and light sources have been widely used for the reduction of the visible signs of photoaging for several years. The benefits of nonablative treatment include quicker patient recovery time due to the absence of marked postoperative erythema, desquamation, and crusting. Moreover, the risks of unwanted pigmentary and textural abnormalities are much reduced in nonablative rejuvenation compared to ablative treatment.

The benefits of nonablative treatment are partially counterbalanced by its reduced efficacy relative to laser skin resurfacing. Among the novel methods for maximizing the efficacy of nonablative treatment is the concurrent use of a photosensitizing agent, such as 5-aminolevulinic acid (5-ALA).<sup>1</sup>

## **5-ALA and Light: Well-Tolerated Treatment of Actinic Keratoses and Photoaging**

Originally developed to be used with red or blue light to treat superficial cutaneous malignancies and premalignant lesions (e.g., actinic keratoses), 5-ALA has recently been applied in combination with a variety of light sources, such as pulsed-dye laser and intense

pulsed light, to increase the effectiveness of light treatment. This cosmetic use entails less intense 5-ALA pretreatment regimens and more well-tolerated light doses for activating the photosensitizer.

This so-called "photodynamic photorejuvenation" was discussed in the literature as early as 2002, when Ruiz-Rodriguez and colleagues<sup>2</sup> treated 17 patients with a combination of actinic keratoses (AKs) and diffuse photodamage. They applied 20% 5-ALA mixed in an oil-in-water emulsion and under occlusion for 4 hours prior to treatment (0.2g/cm<sup>2</sup>) with the pulsed light device (Epilight®, Lumenis), using a 615nm cutoff filter, total fluence of 40J/cm<sup>2</sup> in double pulse mode of 4.0msec with 20msec interpulse delay. Approximately 3/4 of the AKs and adjacent photodamaged skin resolved 1 month after the first treatments, and posttreatment erythema, edema, and crusting lasted up to 10 days.

These results were extended by Alexiades-Armenakas and Geronemus,<sup>3</sup> who showed that photodynamic treatment of AKs could be accomplished gently, not only with intense pulsed light (IPL), but also with 595nm pulsed-dye laser (PDL) (Vbeam®, Candela). The PDL offered the benefits of rapidity of treatment as well as the comfort and protective epidermal effects associated with cryogen spray cooling. The 5-ALA incubation times were as brief as 3 hours and nonpurpuric PDL settings (4-7.5J/cm<sup>2</sup>, pulse duration of 10ms, 10mm spot size, and 30ms cryogen spray with 30ms delay) were used. Minimal intraoperative stinging, burning, and pain were reported, and while there was some postoperative erythema, no purpura, crusting, or scarring was seen. While Alexiades-Armenakas and Geronemus were focused on the treatment of AKs, they demonstrated that laser and 5-ALA could be effectively used with virtually no downtime.

### **5-ALA and Light: Treatment of Photoaging Alone**

Indeed, anecdotal use of IPL and PDL for improvement of the visible signs of aging has rapidly spread. Now the first discrete studies of this application are becoming available. Avram and Goldman<sup>4</sup> retrospectively reviewed 17 patients treated with 5-ALA and IPL and found 55% improvement in telangiectasia, 48% improvement in pigmentary abnormalities, and 25% improvement in coarseness of skin texture, but minimal change in fine wrinkles. Low doses of 5-ALA and IPL permitted post-operative courses significant for only mild erythema and edema for 3-5 days. Separate preliminary studies by both Gold<sup>5</sup> and Roe, et al.<sup>6</sup> have also indicated treatment efficacy following short contact (30-60 minutes incubation) full-face incubation with 20% 5-ALA followed by treatment with IPL.

Recently, a prospective, randomized, controlled trial comparing efficacy and tolerability of 5-ALA followed by IPL treatment with IPL alone was performed by Dover, Bhatia, and Arndt (unpublished data, October 2004). A total of three split-face treatments were delivered to each of 20 patients, and these were followed by two whole-face IPL-only treatments, also 3 weeks apart. Prior to each of the first three treatments, one side of each patient's face was precleansed with acetone and received topical 5-ALA solution for 45 minutes (+15 minutes). The 5-ALA solution was washed off before treatment was commenced with a 560-1200nm device (IPL™ Quantum SR, Lumenis Inc.) using the standard SR head on Program 1 (first pulse of 2.4ms, second pulse of 4.0ms, 14ms interpulse delay; fluence of 23-28J/cm<sup>2</sup>;

epidermal cooling chiller tip on maximum). After each treatment, patients again washed their faces and applied a moisturizer containing an SPF 30 sunscreen. Assessment of outcomes was conducted using a comprehensive rating measure that evaluated global photodamage, fine lines, mottled pigmentation, tactile roughness, and sallowness, each on a 0-4 scale; measurements were obtained by a blinded rater before treatment and 4 weeks after the final treatment. The 5-ALA-IPL sides were associated with 80%-95% improvement on the various subscales compared to 20%-55% improvement for the 5-ALA-only sides. The greatest relative improvements in the 5-ALA-IPL sides were in mottled hyperpigmentation and global photoaging, and to a lesser extent, in fine lines. Tactile roughness and sallowness did not appear to show greater improvement with 5-ALA-IPL treatment vs. IPL alone. Not only the independent rater, but also patients preferred the benefits of the combined 5-ALA-IPL treatment. Significantly, side-effects and tolerability did not differ between the IPL-only treated areas and the areas treated with 5-ALA-IPL.

### **General Treatment Guidelines**

1. IPL (and other light sources, including PDL) can be used after pretreatment with 5-ALA to reduce the visible signs of photoaging.
2. Patients should be instructed that red/brown dyspigmentation and overall appearance are likely to improve significantly, and fine lines, to a lesser extent.
3. Pretreatment with acetone or alcohol is followed by short contact (approximately 1 hour) application of 20% 5-ALA. This is then thoroughly washed off before IPL treatment.
4. IPL or PDL treatment should be delivered at standard parameters.
5. After treatment, the treated area should again be washed off, and moisturizer and sunscreen applied.
6. Patients should be instructed to practice strict sun avoidance and sun protection for the remainder of the treatment day and the next day.
7. Additional treatments are delivered at 3-4 week intervals, with a standard regimen consisting of 3-6 treatments. While it appears from the Dover study that three combined 5-ALA-IPL treatments may produce results as good as or better than five IPL alone treatments, further study is necessary to confirm this finding.

### **Management of Undesired Effects<sup>6</sup>**

The 5-ALA-IPL or PDL treatment for photoaging is a safe treatment associated with patient comfort during treatment and rapid, uneventful recovery after treatment. There are two potential problems that can be easily detected and treated. Phototoxicity occurs when patients disregard instructions regarding post-treatment sun avoidance. The best treatment is prevention, including strict sun avoidance for 24 hours after treatment. If phototoxicity does occur, it presents as well-demarcated erythema and edema at the treated sites. Application of ice and topical corticosteroid ointments, rest, and the passing of time will aid in resolution of symptoms. The risk of superficial infection is very low. Patients with a history of recurrent cold sores may be given antiviral prophylaxis for herpes simplex prior to treatment. Superficial bacterial infections or impetigo may occur at extremely sun-damaged sites or at locations

where the 5-ALA solution has not been completely washed off before IPL treatment. These are typically easily treated with topical antibiotics, such as mupirocin.

## **Conclusion**

Topical 5-ALA enhances the efficacy of laser and light treatment of facial photoaging. While IPL devices have been used most often in this combination therapy, other lasers and light sources, including PDL, appear effective as well. Moreover, combination 5-ALA and light therapy does not add to recovery time or discomfort. Provided sun avoidance is practiced for a day following treatment, combination therapy, like laser or light alone, is associated with mild posttreatment erythema and edema, but no crusting or erosions. The new short-contact regimens of 5-ALA require pretreatment for 30-60 minutes, no longer than the duration of applications of topical anesthetics used for various cutaneous procedures. Finally, prepackaged 20% 5-ALA (Levulan® Kerastick®, DUSA Pharmaceuticals) does not require time-consuming prepara-

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tion prior to application. In short, 5-ALA-light therapy is a further refinement of nonablative laser therapy that permits effective treatment of photoaging with minimization of post-treatment effects.

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