PHOTOREJUVENATION OF FACIAL SKIN WITH TOPICAL 20% 5-AMINOLEVULINIC ACID AND INTENSE PULSED LIGHT TREATMENT: A SPLIT-FACE COMPARISON STUDY

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Abstract

**Background**: Photorejuvenation of facial skin has been reported after intense pulsed light (IPL) therapy alone and in conjunction with topical 5-aminolevulinic acid (5-ALA), but no comparative studies between these regimens have been performed.

**Objective**: To evaluate the safety and effectiveness of combination topical 5-ALA and IPL compared to IPL treatment alone.

**Methods**: Ten patients with mild to moderate photodamage were randomly assigned treatment with 5-ALA + IPL on one facial half and IPL alone on the contralateral side. Two treatments were delivered at 4-week intervals. Clinical improvement scores were determined by masked evaluations of digital photographs obtained at baseline, prior to each treatment session, and at 1, 3, and 6 months after the final treatment.

**Results**: Higher clinical improvement scores were noted on the combination 5-ALA + IPL treated areas. Mild edema, erythema, and desquamation were observed on the facial halves where 5-ALA was applied. No scarring or unwanted pigmentary alteration was seen.

**Conclusions**: Photodynamic therapy with combination topical 5-ALA + IPL is safe and more effective for facial rejuvenation than IPL treatment alone.

Introduction

Photodynamic therapy (PDT) with topical 5-aminolevulinic acid (5-ALA) is an evolving, non-invasive treatment for a variety of dermatologic conditions. Several reports have documented the successful use of PDT in the treatment of acne vulgaris, non-melanoma skin cancers, psoriasis, verrucae, sebaceous hyperplasia, and cutaneous T cell lymphoma.1-11

PDT involves the application of a photosensitizing chemical to a specific cutaneous lesion which, when exposed to visible light, results in excitation of the photosensitizer and consequent production of a reactive oxygen species that leads to cytotoxicity. Topical application of 20% aminolevulinic acid (ALA) initiates time-dependent accumulation of the endogenous photosensitizer protoporphyrin IX (PpIX) in dysplastic and neoplastic dermatologic lesions and epidermal appendages such as sebaceous glands and hair follicles. Since hyperproliferative cells are metabolically more active than normal cells, they convert more ALA to PpIX. PpIX has a large absorption peak in the Soret band (400-430 nm) and smaller absorption peaks at longer wavelengths (509, 544, 584, 630, 690 nm), therefore, many different light sources can be utilized for 5-ALA PDT. Shorter blue light wavelengths are most effectively absorbed by 5-ALA, but have limited skin penetration. On the other hand, the longer yellow and red wavelengths can activate 5-ALA deeper in the skin, potentially reducing the number of treatments needed to exert a positive clinical effect. Treatment discomfort reported during PDT using blue light may also be diminished with the use of longer wavelengths.

Intense pulsed light (IPL) therapy, wherein a light source emits a broad spectrum (515-1200 nm) of wavelengths, has been reported to clinically improve rough texture, dyspigmentation, telangiectasia, and the loss of elasticity associated with photodamaged skin.12-15 While its use with topical 5-ALA also is of apparent benefit for actinic keratoses and photodamage, its relative efficacy to IPL treat-
Table 1. Mean Clinical Improvement.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>1 Month</th>
<th>3 months</th>
<th>6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPL</td>
<td>1.25</td>
<td>1.21</td>
<td>1.28</td>
</tr>
<tr>
<td>IPL + 5-ALA</td>
<td>1.83</td>
<td>1.77</td>
<td>1.65</td>
</tr>
</tbody>
</table>

Quartile grading scale: 1: <25%, 2: 25%-50%, 3: 51%-75%, 4: >75% improvement

The purpose of this study was to evaluate the effectiveness and safety of IPL treatment alone compared to IPL in combination with topical 5-ALA in the treatment of facial cutaneous photodamage.

Materials and Methods
Ten patients (2 male, 8 female, age range 38-63, mean 54.6 years; SPT I and II) with mild to moderate facial photodamage were included for study. No patient received any dermatologic facial treatments for 6 months prior to study entry. Study exclusion criteria included pregnancy or lactation, use of photosensitizing drugs, active infectious disease, or history of photosensitivity.

Facial halves were randomly assigned to receive treatment with the IPL alone or in combination with topical 5-ALA. Topical 20% 5-ALA (Levulan® Kerastick®, DUSA Pharmaceuticals Inc., Wilmington, MA) was uniformly applied to one facial half 60 minutes prior to IPL irradiation. All patients were treated with an IPL source (IPL Quantum SR, Lumenis Corp., Yokneam, Israel) using a 560 nm cut-off filter at energies ranging from 27 to 30 J/cm² (mean: 29.2 J/cm²) with a double pulse of 2.4 msec and 4.0 msec (10 msec delay). All IPL treatments were performed by a single operator using identical technique and protocol. Patients were instructed to use a mild hypoallergenic cleanser and moisturizer, followed by a broad-spectrum sunscreen and strict avoidance of UVA and UVB light for 36 hours after each treatment.

Table 2. Side Effects (20 treatments)

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>IPL</th>
<th>IPL + 5-ALA</th>
<th>Duration</th>
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</thead>
<tbody>
<tr>
<td>Erythema</td>
<td>35%</td>
<td>80%</td>
<td>1-4 days</td>
</tr>
<tr>
<td>Edema</td>
<td>0</td>
<td>30%</td>
<td>48 hours</td>
</tr>
<tr>
<td>Desquamation</td>
<td>0</td>
<td>65%</td>
<td>3-4 days</td>
</tr>
<tr>
<td>Blistering/crusting</td>
<td>0</td>
<td>5%</td>
<td>N/A</td>
</tr>
<tr>
<td>Scarring/dyspigmentation</td>
<td>0</td>
<td>0</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Digital photographs (Mirror Image, Canfield) were obtained using identical camera settings, patient positioning, and room lighting prior to each IPL treatment session and at 1, 3, and 6 months after the final treatment. The degree of clinical improvement of facial photodamage was rated by two independent observers using a quartile clinical grading scale (1: <25% = minimal improvement; 2: 25%-50% = moderate improvement; 3: 51%-75% = marked improvement; 4: >75% = excellent improvement) using comparative photographs to baseline at each treatment and follow-up session.

Results
Greater clinical improvement was noted in the combination topical 5-ALA + IPL-treated facial halves at all postoperative study points (mean clinical grades: 1.82 at 1 month, 1.77 at 3 months, 1.65 at 6 months) than in the facial halves receiving IPL treatment alone (mean clinical grades: 1.25, 1.22, and 1.28 at 1, 3, and 6 months, respectively; Table 1, Figures 1A/B, 2A/B).

Side effects were limited to transient erythema, mild edema, and occasional desquamation, particularly after combination 5-ALA + IPL therapy (Table 2). No scarring or unwanted pigmentary alteration was seen.

Discussion
As public demand grows for less invasive, yet highly effective modalities to address common cosmetic skin concerns, derma surgeons must continue to explore and develop new treatment options and combinations. Intense pulsed light photorejuvenation has been used successfully to improve skin dyspigmentation, texture, and telangiectasia; however, a series of treatments (3 to 6 in succession) are often required to affect significant clinical change.
PDT has been used in the treatment of numerous cutaneous conditions and, more recently, for enhanced photorejuvenation. This study represents the first split-face comparison to demonstrate short-incubation, topical 20% 5-ALA PDT using an intense pulsed light source as an effective, well-tolerated method of photorejuvenation that results in greater clinical improvement than IPL treatment alone. More substantive improvement of skin color, tone, and texture was evident within 2 treatment sessions. The increase in side effects (erythema, edema, desquamation) observed on the 5-ALA + IPL treated areas may render the combination procedure less acceptable by some individuals; therefore, it is essential that the risk of a mild phototoxic reaction be discussed with patients preoperatively.

The exact mechanism by which the addition of 5-ALA enhances photorejuvenation with IPL has not been fully elucidated. It is likely that surface texture and pigmentation improved through mild desquamation. Histological studies have also demonstrated increased fibrosis and new collagen formation in the dermis several months after 5-ALA-PDT for the treatment of basal cell and squamous cell carcinomas. The reason for enhanced treatment of telangiectasia using combined IPL and 5-ALA treatment is unclear. For intravenous or systemic administration of photosensitizers, the highest drug concentrations tend to occur near dermal microvasculature. Topical photosensitizers such as 5-ALA, on the other hand, accumulate predominantly in appendageal structures and hyperproliferative cells.

**Conclusion**

The use of short-incubation topical 5-ALA appears to enhance the effectiveness of IPL treatment for facial photodamage, reducing the number of treatments required for significant clinical improvement. Further study is warranted to optimize treatment protocols through a better understanding of the mechanisms of actions.
References


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