Treatment of Moderate to Severe Inflammatory Acne Vulgaris: Photodynamic Therapy with 5-Aminolevulinic Acid and a Novel Fluorescent Pulsed Light Source

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ABSTRACT

The use of photodynamic therapy (PDT) with 20% 5-aminolevulinic acid (ALA) for the treatment of mild to severe acne vulgaris has been explored by many investigators. This study evaluates the safety and efficacy of a new fluorescent pulsed light source (420-950 nm) for photoactivation in ALA PDT for the treatment of moderate to severe inflammatory acne vulgaris. Nineteen healthy subjects with moderate to severe inflammatory acne of the face received four ALA PDT treatments with a new fluorescent pulsed light source (420-950 nm). Treatments were spaced two weeks apart. ALA incubations times varied from 15 to 30 minutes. At the end of the fourth treatment, the total reductions in inflammatory and noninflammatory lesion counts were 54.5% and 37.5%, respectively. The range of median Global Severity Scores suggest a trend toward reduction after several treatments. Investigator and subject overall assessments show moderate to marked improvement in most patients. The new fluorescent pulsed light source (420-950 nm) for photoactivation in ALA PDT appears to be a safe and effective modality for the treatment of moderate to severe acne vulgaris.

INTRODUCTION

The use of photodynamic therapy (PDT) with 20% 5-aminolevulinic acid (ALA) for the treatment of mild to severe acne vulgaris has been explored by many investigators. The rationale for this approach is based on the update of exogenous ALA by pilosebaceous units, the conversion of ALA to photosensitive protoporphyrin IX (PpIX), the production of porphyrins by Propionibacterium acnes, and the photoexitation of PpIX and bacterial porphyrins to form cytotoxic singlet oxygen. A variety of light sources and lasers have been used for photoactivation of ALA-induced PpIX[1,2,3] and methyl aminolevulinate (MAL) has also been used as photosensitizing agent.[4] A panel of experts has recently agreed that ALA PDT is generally more effective against inflammatory and cystic acne than comedonal acne.[3]

This study evaluates the safety and efficacy of a new fluorescent pulsed light source (420-950 nm) for photoactivation in ALA PDT for the treatment of moderate to severe inflammatory acne vulgaris of the face.

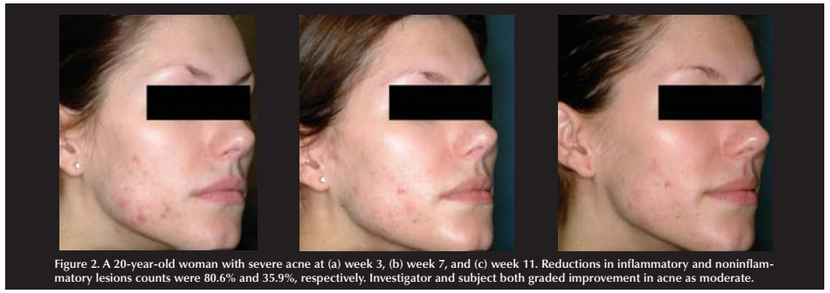

Figure 2. A 20-year-old woman with severe acne at (a) week 3, (b) week 7, and (c) week 11. Reductions in inflammatory and noninflammatory lesions counts were 80.6% and 35.9%, respectively. Investigator and subject both graded improvement in acne as moderate.

MATERIALS & METHODS

Nineteen healthy subjects (aged 19 to 46 years, skin types II-VI, all women) with moderate to severe inflammatory acne of the face (at least 20 inflammatory lesions and a Global Severity Score of 2). The study was approved by the Essex Institutional Review Board, Inc., and all subjects gave signed informed consent to treatment. Subjects were excluded if their histories included previous treatment with laser or light devices or ALA to areas to be treated, severe comedonal acne, autoimmune disease, porphyria or allergy to porphyrins, abnormal photosensitivity, mental illness, topical acne medications within the previous two weeks, systemic antibiotics or steroids within the previous four weeks, systemic retinoids within the previous six months, treatment with an investigational drug within the previous 30 days, dermal filler treatments, botulinum toxin, chemical peels, dermabrasion, keloid or scar formation, uncorrected coagulation defects, or any condition which, in the investigator's opinion, would make it unsafe to participate in this study. Pregnancy or unacceptable methods of birth control were also grounds for exclusion.

At the beginning of the study subjects were given a cleanser to use throughout the study and beginning at least seven days prior to the first study medication application. Subjects were instructed to avoid other cleansers or prohibited topical medications other than the study medications on their face.

The Study Flow Chart is shown in Table 1. Patients received four ALA PDT treatments with a new fluorescent pulsed light source (420-950 nm). Treatments were spaced two weeks apart. ALA incubations times varied from 15 to 30 minutes. Fluences were 5 to 7 J/cm^2, pulse width was 30 to 50 ms, and 5 to 10 minutes of light treatment. The 420 handpiece was used throughout the study and subjects typically received 2 passes at each treatment session.

Results were evaluated by lesion counts, Global Severity Score, improvement scores, adverse effects.

Acne lesions were counted on visits 1-6. Comedones (open and closed), papules, and pustules, and nodules were counted and recorded on the face vertically from hairline to mandible rim and horizontally from ear to ear.

A Global Severity Score was assigned to each subject on visits 1-6. The scale was 0 to 3 in which 0 = clear, no lesions; 1= mild, <10 inflammatory lesions; 2 = moderate, ~20 inflammatory lesions; and 3 = severe, >40 inflammatory lesions localized or scattered. Enrolled subjects had a Global Severity Score at least 2 at visit 1.

Improvement was assessed by comparing facial acne to visit 1. Improvement grades were assigned as follows: 0 = none; 1 = slight (25%); 2 = moderate (50%); 3 = marked (75%); 4 = complete clearing (95%).

Adverse effects (mottled hyperpigmentation, erythema, edema, stinging (before and after treatment), and crusts and erosions were graded on a scale of 0 to 3 with 3 as most severe.

Overall improvement was assessed by the investigator and by subjects on visits 5 and 6.

Table 1. Study Flow Chart

Procedure	Screening	Visit 1 (wk 1)	Visit 2 (wk 3)	Visit 3 (wk 5)	Visit 4 (wk 7)	Visit 5 (wk 11)	Visit 6 (wk 19)
Clinical evaluation	X	X	X	X	X	X	X
Treatment		X	X	X	X		
Adverse events		X	X	X	X	X	X
Subject evaluation					X	X	X

RESULTS

Fifteen of the 19 subjects completed the study up to visit 5. One was lost to follow-up and the remaining three withdrew consent. Since 4 of the 15 patients who completed the study up to visit 5 provided data for all parameters at visit 6 (week 19), the data from visit 6 is not included in the analyses.

Lesion counts

The reductions in both inflammatory and noninflammatory lesion counts in shown in Figure 1.

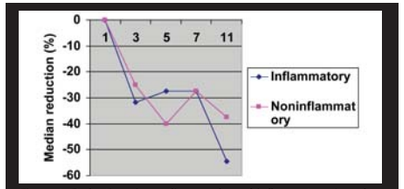

Figure 1. Reductions in median number of inflammatory (papules, pustules, nodules) and noninflammatory (comedones, open and closed) lesion counts from week 1. Treatments were given on weeks 1, 3, 5, and 7. The greatest reductions occurred after the first treatment in both types of lesions. Improvement appears to level off, then continue for at least four weeks after the final treatment. At the end of week 11, the total reductions in inflammatory and noninflammatory lesion counts were 54.5% and 37.5%, respectively.

The median (96.6% CI, n=15) Global Severity Score at weeks 1, 3, and 5 were 2.0 (2.0-2.0) and 2.0 (1.0-2.0) at weeks 7 and 11. The extension of the lower limit of the range from 2.0 to 1.0 at weeks 7 and 11 suggests a trend toward reduction in Global Severity Score, although the medians remain constant.

Improvements in weeks 3, 7, and 11 for two patients are shown in Figures 2 and 3.

The median (96.5% CI) investigator-assessed improvement score was 2.0 (1.0-2.0), slightly lower than the corresponding subject-assessed 2.5 (2.0-3.0) at visit 5.

The adverse effect data are shown in Table 2.

Table 2. Median (96.5% CI) severity of adverse effects during visits 1-5 (weeks 1-11)

Adverse effects	Visit 1 (WK) 1 (1)	2 (3)	3 (5)	4 (7)	5 (11)
Mottled hyperpigmentation	0.0 (0.0-1.0)	0.0 (0.0-1.0)	1.0 (0.0-1.0)	1.0 (0.0-1.0)	1.0 (0.0-2.0)
Erythema	0.0 (0.0-1.0)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	0.0 (0.0-1.0)
Stinging (pretreatment)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	—
Stinging (posttreatment)	2.0 (1.0-2.0)	2.0 (1.0-2.0)	2.0 (1.0-2.0)	2.0 (1.0-2.0)	—

Mottled hyperpigmentation increased slightly by the third treatment (visit 3) and again by visit 5, four weeks after the final treatment as suggested by the extension of the upper limit of the 96.5% CI from 1.0 to 2.0. Erythema and pretreatment stinging (while ALA incubated) were slight (0.0 and 1.0, respectively) and did not change throughout the course of treatment. Posttreatment stinging was greater (2.0 [1.0-2.0]) than pretreatment stinging, but did not become more severe with continued treatment.

DISCUSSION

The results show that ALA PDT with the novel fluorescent pulsed light source (420-950 nm) for photoactivation is a safe and effective treatment of moderate to severe acne. As in earlier studies with ALA PDT for acne, lesion count reduction is greater for inflammatory lesions than for noninflammatory lesions.[3]

The use pulsed light with ALA PDT for the treatment of acne vulgaris has been reported in two studies.[5,6] In Gold's study of 12 patients responding to ALA PDT with intense pulsed light (IPL) and a heat source, reduction in inflammatory lesions was 50.1% after 4 once-weekly treatments, 68.5% four weeks later, and 71.8% 12 weeks after the final treatment. In the present study, the reduction in inflammatory lesion counts was 54.5%, slightly higher than the 50.1% reported earlier. Unlike the present study, a heat source was also used and the treatments were given one week apart rather than two weeks apart. ALA contact time was 1 hour, more than twice as long as the 15 to 30 minutes ALA contact time in the present study. Fluences and pulse durations used in the earlier study were 3 to 9 J/cm^2 and 35 ms, respectively, similar to 5 to 7 J/cm^2 and 30-50 ms settings used in the present study. In both studies, the treatments were well tolerated.

In a split-face study of patients with various degrees of acne, Santos and colleagues[6] treated one side of the faces with ALA PDT and IPL and the other side with IPL alone. Two treatments were given spaced two weeks apart. ALA was incubated 3 hours and fluences started at 26 J/cm^2 and were increased to 34 J/cm^2. Treatment was given in double pulses (2.0 and 6.0 ms). After two treatments, visible improvement was apparent in most patients on both sides of the face, with the ALA PDT side showing greater improvement. Results were evaluated by a subjective grading system and lesion counts were not reported.

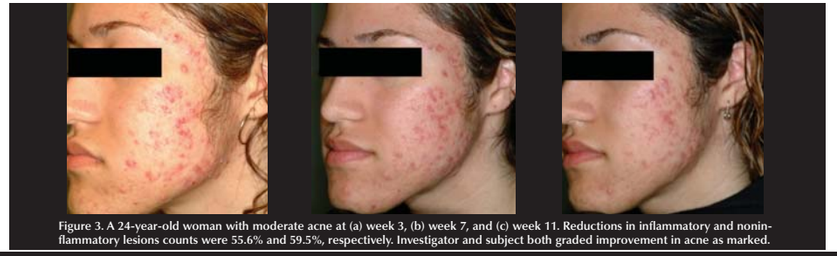

Figure 3. A 24-year-old woman with moderate acne at (a) week 3, (b) week 7, and (c) week 11. Reductions in inflammatory and noninflammatory lesions counts were 55.6% and 59.5%, respectively. Investigator and subject both graded improvement in acne as marked.

CONCLUSION

The new fluorescent pulsed light source (420-950 nm) for photoactivation in ALA PDT appears to be a safe and effective modality for the treatment of moderate to severe acne vulgaris of the face.

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