Topical Aminolaevulinic Acid-Photodynamic Therapy for the Treatment of Mild to Moderate Inflammatory Acne

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Background: **Photodynamic therapy (PDT) using aminolevulinic acid (ALA) is a new technique. PDT is being studied extensively and is used in a variety of dermatology settings.**

Objective: **The purpose of this study was to evaluate the safety and efficacy of topical ALA-PDT in patients with mild to moderate inflammatory acne.**

Method: **Ten patients were enrolled in a clinical trial to evaluate ALA-PDT with activation by intense pulsed light. They were given a 20% topical ALA photosensitizing agent that remained in contact with the skin for 60 minutes before irradiation. No additional treatment was provided after PDT.**

Results: **The Korean acne grading system was used for clinical assessment. Our results showed a statistically significant clinical improvement of the inflammatory acne at eight weeks after two sessions of treatment. Side effects such as slight discomfort, burning and stinging were reported during the irradiation.**

Conclusion: **ALA-PDT is a safe and effective treatment modality for inflammatory acne. (Ann Dermatol (Seoul) 19(2) 55～59, 2007)**

Key Words: Acne, Aminolevulinic acid, Intense pulsed light, Korean acne grading system, Photodynamic therapy

INTRODUCTION

Photodynamic therapy (PDT) using aminolevulinic acid (ALA) is a new technique. PDT is being extensively studied in a variety of dermatology settings[1-4]. These applications include FDA approved treatment of premalignant and malignant skin conditions, as well as off-label uses for photorejuvination[3-5] and the treatment of acne vulgaris[2,4,6-8], sebaceous gland hyperplasia[9], telangiectasia[10], rosacea[1,11], and hirsutism[1,3,12-14]. There are three possible modes of action suggested for ALA-PDT use in acne: photodynamic destruction of *Propionibacterium acne* by sterilizing the sebaceous follicle, direct photodynamic injury of the sebaceous glands inhibiting sebum production and reduction of follicular obstruction by effects on keratinocyte shedding and hyperkeratosis[8].

ALA is known to be preferentially taken up by the pilosebaceous unit, which is metabolized by heme synthesis to produce a precursor of protoporphyrin IX, a potent photosensitizer[15]. The ALA-PDT procedure has potential to provide a unique treatment for acne by selectively damaging the pilosebaceous unit with little damage to the surrounding skin.

We have designed a pilot study using topical ALA-PDT to treat 10 patients with mild to moderate acne. The purpose of this study was to evaluate the safety and efficacy of ALA-PDT.

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MATERIALS AND METHOD

Materials

We studied 10 healthy subjects of both genders (6 women, 4 men) with an age range of 20 to 29 years (mean age 24.7 years) with acne vulgaris on

the face (KAGS; Korean acne grading system grade 3-5). They were enrolled from March 2005 to April 2005. All patients were Fitzpatrick photo skin type II-III and their degree of pigmentation varied from light to medium. Exclusion criteria included serious intercurrent illness, infections, pregnancy or lactation, women of childbearing age not using effective contraception, systemic antibiotics taken in the past two weeks, or systemic retinoids used in the past one year. Any patient with a photosensitivity disorder and those planning excessive sun light exposure were also excluded. All patients gave informed consent for the procedure and alternative treatments were discussed.

Method

The area to be treated was prepared with 70% alcohol to enhance ALA penetration; then 20% ALA (5-ALA®; Medac, Wedel, Germany + Base Sama oint®; Samapharm, Seoul, Korea) was applied for 60 minutes under an occlusive dressing with plastic film. Application of a wavelength band ranging from 530 nm to 720 nm was used a taking advance of the principle of dual mode filtering. The average energy level was 8.5-11.0 J/cm^2 (mean 9.4 J/cm^2) given by intense pulsed light (Ellipse®; DDD, Horsholm, Denmark). All patients underwent two sessions of PDT at four-week intervals. A single operator used identical techniques and protocols for all treatments. Patients were instructed to use a broad-spectrum sunscreen and to avoid UVA and UVB light for 24 hours after each treatment. Each subject's acne was visually assessed at baseline and eight weeks after the second treatment, using the KAGS criteria for acne. At the follow-up visit, all patients were placed in front of a mirror with built in illumination. They were asked to evaluate the outcome based on comparison with photos taken before treatment. The presence of patient side effects was evaluated at every visit. Routine hematological, hepatic, and renal function studies and urinalysis were performed at baseline and the study endpoint.

The statistical analysis performed was the Wilcoxon signed rank test used to compare baseline changes in acne lesion count.

RESULTS

Clinical evaluation

All 10 subjects completed the study. There was a statistically significant reduction in the inflammatory acne lesion count at eight weeks after two sessions of treatment (Table 1) compared to the baseline. Three dermatologists, unaware of the status of treatment, globally assessed clinical improvement;

Table 1. Clinical evaluation by Korean acne grading system

Patient	Sex /age	KADG (pretreatment)			KADG (posttreatment)		
		Grade	Papule	Nodule	Grade	Papule	Nodule
1	F/22	3	36	4	2	16	0
2	M/24	4	21	12	3	22	4
3	M/21	4	42	13	2	9	0
4	F/20	3	39	5	1	10	0
5	F/29	3	45	7	2	25	0
6	M/29	4	38	18	2	15	0
7*	M/25	5	47	28	3	32	6
8	F/24	3	51	9	2	28	0
9	F/25	3	48	8	2	24	0
10	F/28	3	34	4	2	16	0

*: The subject was seen superficial exfoliation but spontaneous healing without scarring within 2 weeks.

they graded the acne changes without knowledge of the clinical factors. The treated area was noted to have improved at visit one (week 1) and this improvement continued throughout the follow-up period (up to 12 week at least). The effects were determined based on comparisons of the assessed grades at baseline (Fig. 1) compared to the eight-week follow-up visit (Fig. 2) after the second treatment. Using the Wilcoxon signed rank test the differences were significant ($p<0.002$). There was also a reduction in the noninflammatory lesion counts at the ALA-PDT site; but these changes did not reach statistical significance. The study subjects scored their overall satisfaction with the treatment, and 76.2% of the patients rated the treatment as either good or excellent.

Adverse effects

All subjects experienced a mild tingling or burning after two to three minutes of the treatment, which did not alter or worsen subsequent treatment. Patients reported side effects including discomfort or mild burning (n=8), stinging or pruritus (n=6) and acute pain necessitating analgesics (n=1). Local edema and transient erythema usually occured for approximately 24 hours after light exposure. Transient hyperpigmentation (n=7) and mild perifollicular eruption (n=4) subsided within two hours; mild crusting (n=2) and superficial exfoliation (n=1) were observed and cleared without scarring. There were no significant abnormalities in the laboratory tests during and after treatment.

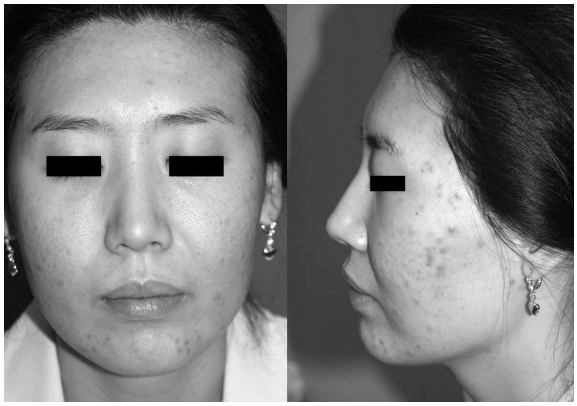

Fig. 1. Patient 1. pretreatment state.

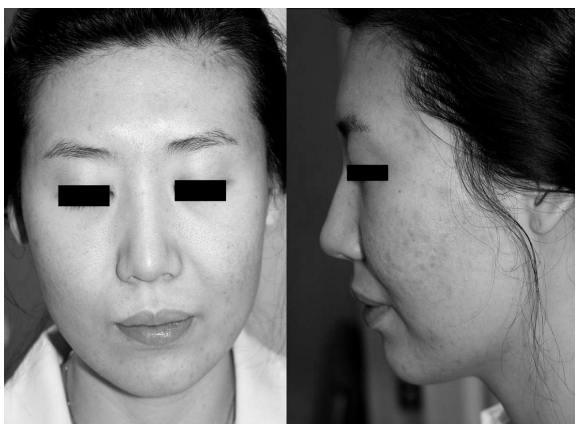

Fig. 2. Patient 1. posttreatment 8 weeks.

DISCUSSION

Beginning with Kennedy's pioneering studies[16], topical ALA has been studied in skin because it is a nontoxic, naturally occurring substance that targets cells involved in porphyrin synthesis. This new photosensitizing drug has the ability to penetrate the stratum corneum in a variety of skin tumors, basal cell carcinomas, solar keratoses, and squamous cell carcinoma as well as sebaceous glands. Topically applied ALA to photo-aged and photo-damaged skin leads to the accumulation of the photosensitizer, which is activated by exposure to light, and decrease sun-induced, uneven skin pigmention changes and disorders of the pilosebaceous unit[1,4,8].

Hongcharu et al.[6] reported on the use of 5-ALA-PDT for the treatment of acne vulgaris of the back in 22 patients utilizing broadband light and three-hour drug incubation. Significant clinical and statistical improvement of the acne scores were noted after four weekly treatments in all patients compared to control areas; these results persisted for up to 20 weeks. Adverse effects included acneiform folliculitis, postinflammatory hyperpigmentation, superficial peeling and crusting. Itoh et al.[19] reported on an intractable case of acne vulgaris on the face that was treated with 5-ALA PDT after four-hours of drug incubation and a 635nm pulsed excimer-dye laser. The treated area remained clear during the eight-month follow-up period. Erythema and edema were observed after therapy followed by crusting until the areas healed at 10 days. Goldman[20] has reported on short contact (15-minute drug incubation) 5-ALA PDT and an intense pulsed light device or blue light for the treatment of acne vulgaris

and sebaceous hyperplasia. Treatment was noted to be pain-free and without adverse effects. Relative clearing of the acne vulgaris was observed after two to four weekly treatments. Gold[21] evaluated 10 patients with moderate to severe acne vulgaris utilizing short-contact (30-minute to 1-hour drug incubation) 5-ALA PDT and the blue light system. Four weekly sessions resulted in a response of approximately 60% that persisted till a three-month post-therapy treatment follow-up. Sessions were well-tolerated with no adverse effects. Therefore, in our study, we chose to use 1-hour ALA incubation.

The results of our study suggest that ALA-PDT with IPL for drug activation is a promising option for acne treatment. Additional studies to optimize ALA-PDT treatment strategies are warranted. For example, preoperative degreasing with 70% alcohol prior to the application of ALA may enhance penetration and result in better outcomes. In addition, frequent treatments at shorter intervals may also improve results. We did nothing in this study to optimize or alleviate the side effects of ALA-PDT. It is unlikely that we by chance used the best conditions of PDT for acne. The dose-response characteristics of ALA-PDT treatment for acne are unknown. Therefore, these and other ideas may be worth pursuing because it is now clear that acne vulgaris responds to ALA-PDT.

As patient requests for less invasive treatment increase and highly effective treatments for common cosmetic skin conditions expand, dermatologists continue to explore and develop new treatment modalities. However, the series of sequential treatments and the high cost of ALA are a burden for some patients. As improved photosensitizers and less expensive light sources are developed, PDT will undoubtedly become a more commonly used alternative for the treatment of a variety of facial epidermal and pilosebaceous disorders.

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