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Acne phototherapy with a high-intensity, enhanced, narrow-band, blue light source: an open study and in vitro investigation

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Abstract

The purpose of this study was to investigate the efficacy of phototherapy with a newly-developed high-intensity, enhanced, narrow-band, blue light source in patients with mild to moderate acne. An open study was performed in acne patients who were treated twice a week up to 5 weeks. Acne lesions were reduced by 64%. Two patients experienced dryness. No patient discontinued treatment due to adverse effects. In vitro investigation revealed that irradiation from this light source reduced the number of *Propionibacterium acnes (P. acnes)*, but not *Staphylococcus epidermidis* that were isolated from the acne patients. Phototherapy using this blue light source was effective and well tolerated in acne patients and had an ability to decrease numbers of *P. acnes* in vitro, suggesting that this phototherapy may be a new modality for the treatment of acne.

Keywords: Acne vulgaris; Phototherapy; Blue light; *Propionibacterium acnes*

1. Introduction

Sun exposure is known to be beneficial for acne vulgaris [1]. Ultraviolet (UV) light [2–5], visible light [6,7], and the combination of UVA plus visible light [8–10] have been reported to be effective for acne vulgaris. *Propionibacterium acnes* (*P. acnes*) produces porphyrins [11–15] of which absorption spectra is in the near UV and blue light spectrum. The main porphyrin produced by *P. acnes* is coproporphyrin III of which absorption spectrum peak is at 415 nm [12,13]. Blue light, therefore, is a theoretically effective phototherapy since exposure to blue visible light induces photoexcitation of bacterial porphyrins, singlet oxygen production, and subsequent bacterial destruction [16].

Recent reports demonstrate that the visible light with peaks at 405 and 420 nm [6] and the combination of blue (415 nm) and red (660 nm) light [7] are clinically effective in acne vulgaris.

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However, they used low-intensity fluorescent lamps as a light source. In this investigation, we performed an open study of a newly-developed high-intensity, enhanced, narrow-band (407–420 nm), blue light source using metal halide lamp, as blue light phototherapy of acne vulgaris. The bactericidal effects of this light source on isolates from the lesions of acne patients were also tested. This blue visible light source was shown to be effective and well tolerated by acne patients and had a reducing activity of numbers of *P. acnes*, suggesting that this blue light therapy could be a possible new treatment modality for acne.

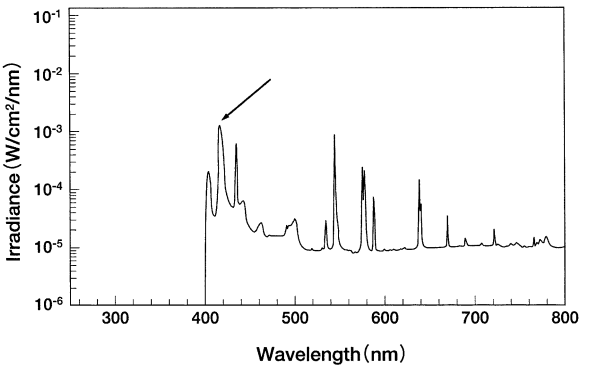


Fig. 1. Spectral irradiance of the blue light source. An arrow indicated the emitting peak.

2. Patients and methods

2.1. Patients

This study was an open clinical trial performed at our department from February to October 2001. Thirty patients, 27 females and 3 males, with mild to moderate acne lesions involving the face and/or the back and/or the chest participated in this study. Mild to moderate acne was determined according to Glass's definition [17]. To be included, patients had to have between 15 and 100 inflammatory lesions and/or between 15 and 100 non-inflammatory lesions and no more than 3 nodules [17]. The average age was 22 years (female, 22 years, range 18–41; male, 24 years, range 22–27). During the 4 weeks prior to the study, no medication was administered. The aims of the study were explained to the patients, and they gave informed consent.

2.2. Treatment protocol

A high-intensity, enhanced, narrow-band, blue light source (ClearLight^{TM}, Lumenis, Tokyo) was used for all treatments. This apparatus had each 400-W metal halide lamp (SA5530000, Lumenis) plus double UV-cut filters with the emitting peak of 407–420 nm for lesions of right or left side of the face. The spectral irradiance was shown in Fig. 1. Treatment fluence was 90 mW/cm^2 of visible light over an area of 20 $\times$ 20 cm^2. Each patient received treatments twice a week up to 5 weeks, during which time any other acne therapy was prohibited. During the treatment, both eyes of patients were protected with a visible light protected eyeglass to prevent unexpected adverse effects of visible light.

Clinical assessment was performed 4 times during the trial period (0, 1, 3 and 5 weeks) and at 1 month after the final treatment. First, the number of lesions e.g. comedones, papules, and pustules, was counted. The secondary criterion was the investigator's global improvement rating on a five-point scale (-1 = worsened, 0 = unchanged, 1 = improved, 2 = markedly improved, and 3 = resolved). Tolerance was assessed by asking patients about any signs or symptoms of adverse reactions.

2.3. Bacterial culture

The broth dilution method was used as described previously [18]. Briefly described, the contents of acne lesions of patients were obtained before treatment, and were homogenized, diluted, and inoculated into the appropriate media. After incubation both aerobically and anaerobically, organisms were identified.

2.4. In vitro irradiation

Each 5 strains isolated from randomly-selected acne patients were used to assess the bactericidal ability of irradiation from this light source. Bacteria with certain number were diluted in

ABCM or Mueller-Hinton broth, contained in a translucent glass bottle with some air, and exposed to the light source for 60 min at a distance of 25 cm. Fluence was 90 mW/cm^2 and total energy dose of 60-min irradiation was 324 J/cm^2. Immediately and at 60 min after the irradiation, the number of bacteria cultured in *Brucella* HK or blood agar medium was counted. The numbers of cultured bacteria of pre- and non-irradiation were also calculated.

3. Results

3.1. Patients

Thirty patients were recruited for the study. Three patients discontinued treatment with a complaint of worsening of skin lesions and 1 patient stopped for non-medical reasons. The numbers of comedones, papules, pustules, and comedones+papules+pustules (mean±SD) before the treatment were 22.0±16.4, 18.9±11.3, 4.7±7.9, and 45.5±25.6, respectively.

3.2. Clinical efficacy

Twenty-six patients completed the study. Two patients showed cleared by week 3. Three patients who discontinued the treatment were confirmed to be worsened by the investigator. At 1 week, the number of comedones, papules, pustules, and comedones+papules+pustules (mean±SD) was 16.7±13.4, 10.9±7.4, 2.8±4.3, and 30.4±19.2, respectively. At 3 weeks, the numbers (mean±SD) were 12.0±11.8, 7.7±5.6, 2.5±2.9, and 22.2±17.3, respectively. At 5 weeks, the numbers (mean±SD) were 9.3±9.6, 5.8±4.5, 1.3±2.0, and 16.4±12.9, respectively. Thus, blue light therapy in our study achieved a marked reduction of comedones, papules, pustules, and comedones+papules+pustules by 45.5, 59.3, 46.8, and 51.2% at 3 weeks, as well as by 57.8, 69.3, 73.3, and 64.0% at 5 weeks, respectively (Fig. 2). Assessment of efficacy by the investigators showed that 77% of the patients were improved by week 5, while 10% demonstrated 'unchanged' (Table 1). By week 5, 40% of the patients showed marked improvement or clearance of their acne lesions (Table 1). Clinical pictures of 2 patients with marked improvement were shown as Fig. 3 and Fig. 4.

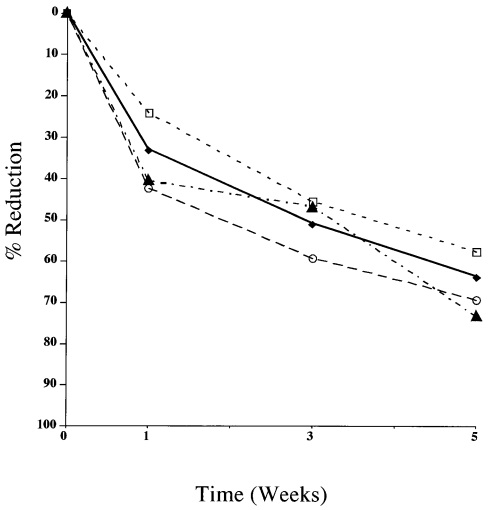
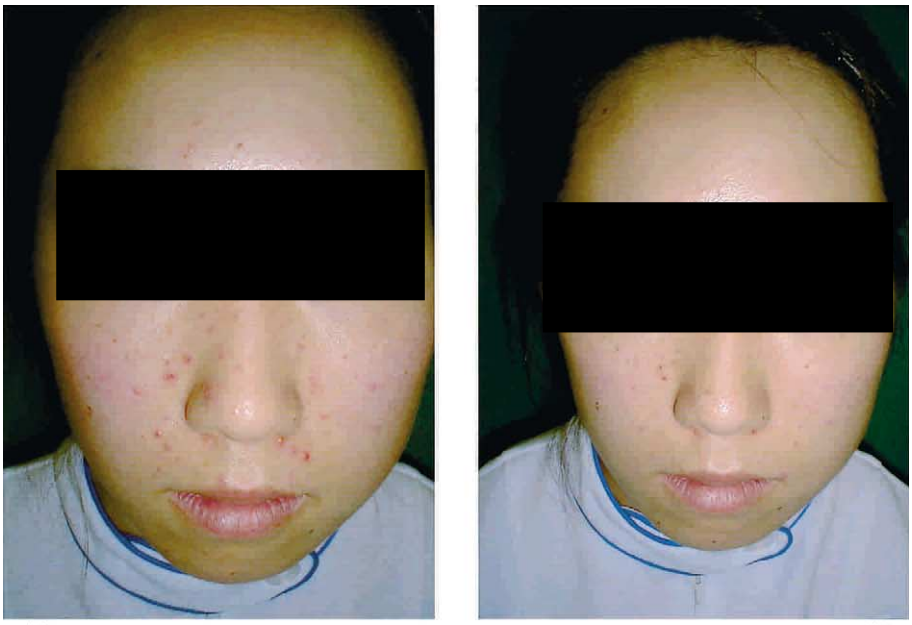


Fig. 2. Counts of lesions (mean percentage reduction). Comedones (□), papuples (○), pustules (▲), and comedones+papuples+pustules (◆).

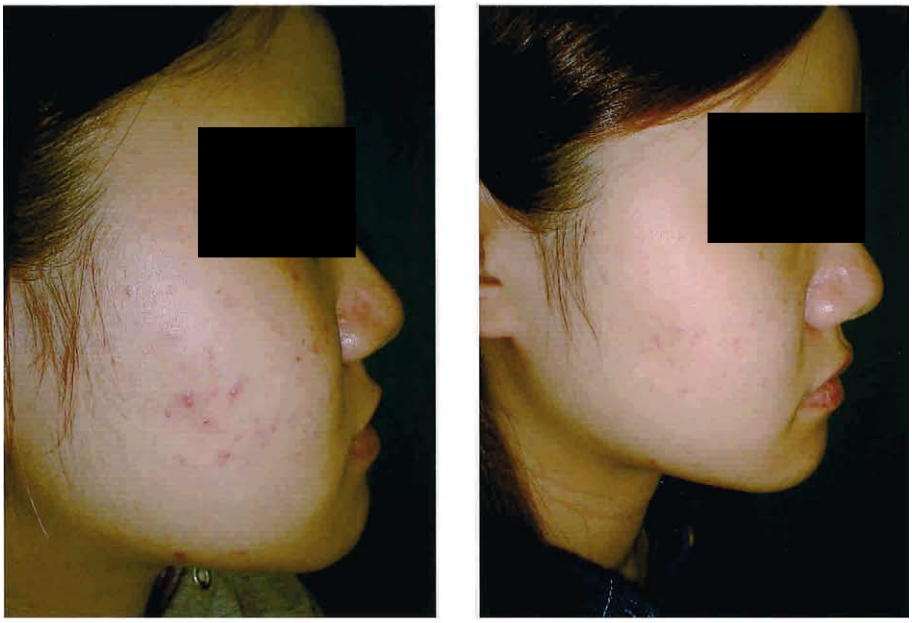
Table 1
Physician's overall ratings for the response of inflammatory acne

Rating	Number (%)
ND	1 (3)
Worsened	3 (10)
Unchanged	3 (10)
Improved	11 (37)
Markedly improved	9 (30)
Resolved	3 (10)
Total	30 (100)

Durability of clinical improvement was studied in 17 patients who came to our department at 1 month after the treatment. During 1 month any treatment was prohibited for acne. At the end of treatment, the number of comedones, papules, pustules, and comedones+papules+pustules (mean±SD) was 9.8±10.0, 5.5±5.1, 1.1±1.9, and 16.4±14.0, respectively. At 1 month after the final treatment, the number of comedones, papules, pustules, and comedones+papules+pus-



(a) Fig. 3 (b)



(a) Fig. 4 (b)

Fig. 3. Case 1 (female, 22 years) with marked clinical improvement. a, before, and b, after the treatment.
Fig. 4. Case 2 (female, 20 years) with marked clinical improvement. a, before, and b, after the treatment.

tules (mean ± SD) was 9.7 ± 10.1, 5.8 ± 5.1, 1.6 ± 2.0, and 17.1 ± 14.3, respectively. The increase of total number was 6%, suggesting that this therapy may have good durability within 1 month after the treatment.

3.3. Tolerability

Dryness of irradiated skin was seen in 2 of the patients and no patient discontinued treatment due to adverse effects.

3.4. Bacterial isolates

Only one of 24 samples was negative after culture. As shown in Table 2, 21 strains of *P. acnes* and 20 strains of *Staphylococcus* (*S.*) *epidermidis*, were major isolated bacteria, with *P. acnes* and *S. epidermis* being isolated simultaneously from 18 specimens. Each 1 strain of methicillin-sensitive *S. aureus* (MSSA), methicillin-resistant *S. aureus* (MRSA), *S. xylosus*, *S. capitis*, and *S. hominis* was isolated. Patients who had MSSA and MRSA discontinued the treatment with the complaint of 'worsened' that was also confirmed by the investigator to be worsened.

3.5. Bactericidal effects in vitro

As shown in Table 3, *P. acnes* was decreased in number after irradiation whereas *S. epidermidis* was not. *P. acnes* cultured at 60 min after irradiation demonstrated significant reduction ($P < 0.05$) using Student's t-test.

Table 2
Species of bacterial isolates

Species	Number
P. acnes	2
P. acnes + *S. epidermidis*	14
P. acnes + *S. xylosus*	1
P. acnes + *S. epidermidis* + MSSA	1
P. acnes + *S. epidermidis* + MRSA	1
P. acnes + *S. epidermidis* + *S. capitis*	1
P. acnes + *S. epidermidis* + *S. hominis*	1
S. epidermidis	2
Negative	1

MSSA, methicillin-sensitive *S. aureus*; MRSA, methicillin-resistant *S. aureus*.

Table 3
Numbers of cultured bacteria ($\times 10^9$) of pre-, post-, and non-irradiation of ClearLight

	Pre-irradiation	Post-irradiation	Non-irradiation
P. acnes			
Immediately	5.1 ± 1.4	4.3 ± 1.4	4.8 ± 1.4
60 min after	4.1 ± 0.8	3.1 ± 0.8*	3.8 ± 0.9
S. epidermidis			
Immediately	3.8 ± 1.6	3.7 ± 1.3	3.7 ± 1.6
60 min after	1.9 ± 0.6	2.0 ± 0.5	1.8 ± 0.4

* $P < 0.05$ compared with pre-irradiation.

4. Discussion

The blue light source in our study demonstrated a marked effect on mild to moderate acne lesions as well as being well tolerated. The reduction of number of skin lesions was 51.2% at 3 weeks and 64.0% at 5 weeks. Seventy-seven percent of the patients showed improvement by week 5 although 20% of the patients worsened or unchanged. Only 2 patients complained dryness of the skin and completed the study. The durability of clinical improvement was examined in 18 of 26 patients who completed the treatment and proved to be effective at least by 1 month. This good durability may suggest that the blue light phototherapy can prolong the occurrence of acne lesions. Therefore, blue light may be added to the panel of phototherapy used for acne treatment. However, a longer follow-up study, e.g. more than 3 months, is necessary in order to reveal the advantage of this therapy compared with classical acne treatments and is currently under way.

This blue light therapy had fewer effects for comedones (57.8% reduction) than inflammatory papules (69.3%) and pustules (73.3%). Previous studies [6,7] using blue light also show less improvement in comedones than inflammatory lesions. Blue light therapy may be more effective for inflammatory acne because of antibacterial

activity against *P. acnes*. Comedolytic agents should be used in patients who have predominantly comedones.

Photodynamic therapy using topical or systemic 5-aminolevulinic acid (ALA) has been widely used for the treatment of cancers including non-melanoma skin cancers. ALA-based photodynamic therapy utilizes visible light-induced phototoxic reaction of ALA-derived protoporphyrin IX (PpIX) accumulated in the target lesions [19]. Systemic administration of ALA induces phototoxic damage to sebaceous glands and hair follicles in mice [20]. Topical ALA-photodynamic therapy is effective for acne vulgaris with significant side effects such as transient hyperpigmentation, superficial exfoliation, and crusting [21]. However, the techniques of topical ALA-photodynamic therapy for skin disorders have not been optimally established since inhomogenous distribution or lack of selective accumulation of ALA-derived PpIX [19]. Blue light therapy for acne may be a kind of photodynamic therapy using endogenous porphyrins produced by *P. acnes*. Therefore, this blue light is highly selective for acne lesions and seems to have minimal adverse effects on normal skin. Under our condition, almost no adverse effects except dryness of the skin were found.

P. acnes is mainly implicated in the pathogenesis of inflamed lesions of acne vulgaris [22]. There is a correlation between reduction in number of *P. acnes* and clinical improvement in patients with acne [23]. However, *S. epidermidis* is frequently cultured with *P. acnes* simultaneously in 54–57% of acne patients [18,24]. In our study, *S. epidermidis* was co-cultured with *P. acnes* in 18 (78%) of 23 samples. In vitro study showed the reducing effect of irradiation from this light source for *P. acnes*, but not for *S. epidermidis*. Hence, the clinical effects shown in this study may have been achieved due to the bactericidal activity of the irradiation from this blue light source on *P. acnes* from acne patients. More investigation is needed to clarify the relationship between clinical effects and in vitro activity, since in vivo and in vitro conditions were quite different.

Two patients in our study who showed MSSA or MRSA co-cultured with *P. acnes* and *S. epidermidis* discontinued the study because of ineffectiveness of phototherapy. The main pathogen in acne lesions of these patients may have been *S. aureus* that did not respond to blue light. Appropriate antibiotics should be administered in these cases. It may be advisable to test cultured bacteria prior the treatment. If the patients from whom *P. acnes* was cultured were selected, the more improvement may be achieved. Further study is needed to evaluate the relationship between cultured bacteria and clinical improvement.

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