

## Blue light phototherapy in the treatment of acne

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**Background:** Blue light irradiation is known to be effective against acne. However, the profile of a good candidate is still unclear.

**Methods:** Thirty-one Taiwanese with symmetrical facial acne were irradiated with blue light on one side of the face selected randomly twice weekly for 4 consecutive weeks. The other half of the face was left untreated as control. Parameters, including scar type, pore size, and facial follicular porphyrin fluorescence intensity, were documented. The severity of acne was assessed before the treatment, after two, four, and eight sessions of treatment, and 1 month after the treatment was completed.

**Results:** Compared with the non-irradiation side, eight sessions of blue light irradiation were effective in acne treatment ( $P < 0.001$ ). Gender ( $P = 0.471$ ),

scar type ( $P$ -values of pitted, atrophic, and hypertrophic type were 0.688, 0.572, and 0.802, respectively), pore size ( $P = 0.755$ ), and pretreatment fluorescence intensity ( $P = 0.656$ ) could not be used as predictive factors of therapeutic effectiveness. Compared with pretreatment, nodulocystic lesions tended to worsen despite treatment. In addition, the therapeutic effectiveness was not related to the fluorescence intensity change ( $P = 0.812$ ).

**Conclusions:** Blue light irradiation is effective in acne treatment. Patients without nodulocystic lesions are better candidates for blue light irradiation.

**Key words:** acne vulgaris; blue light; fluorescence; *Propionibacterium acnes*.

Acne vulgaris is a common disorder that causes great cosmetic concern, especially among young people. If it is not treated properly, permanent scarring can ensue. Although isotretinoin is effective for intractable acne, side effects and teratogenicity limit its use (1–3). On the other hand, antibiotics, which suppress *Propionibacterium acnes*, are the standard treatment for acne but are becoming less effective probably because of the emergence of antibiotic-resistant strains (4–7). An alternative option for acne treatment is desirable. In the past few years, more and more evidence has shown that blue light irradiation is effective against acne (8–10). However, the profile of a good candidate for blue light irradiation is still not well characterized. In addition, based on *in vitro* observation, *P. acnes* containing fluorescent porphyrins can be killed by a blue light-induced photodynamic effect (11–13). If this also holds true *in vivo*, we can expect that acne patients with more facial *P. acnes* colonies will respond better to the blue light treatment. To further clarify the therapeutic role of blue light, we irradiated acne patients with blue light and observed the change in facial fluorescence intensity at the same time.

### Patients and methods

#### Patients

Thirty-one Taiwanese, skin type III–IV, with mild-to-moderately severe acne vulgaris symmetrically on their face were enrolled after they had given their informed written consent. Only those who met the following criteria were included: (1) neither topical nor systemic antibiotics had been used in the previous 2 weeks; (2) not on medication that exacerbates or alleviates acne; (3) not planning to have excessive sunlight exposure; (4) no history of keloid or photosensitivity disorders; and (5) not pregnant or lactating. In addition, no other active treatment was allowed during the treatment and within 1 month after the treatment was completed.

#### Study design

After a gentle facial wash and eye protection with goggles, patients, were irradiated with blue light on one side of the face twice weekly for four consecutive weeks. The side of irradiation was randomly assigned for each patient. The blue light had a symmetrical peak wavelength of  $420 \pm 20$  nm (F-36 W/Blue V, Waldmann, Villingen-Schwenningen, Germany). At a

distance of 15 cm, the irradiation dose of blue light each time was 40 J/cm<sup>2</sup>.

#### Clinical assessments

Each subject's acne was visually assessed during the treatment and at 1-month follow up, using an acne score modified from that previously described by Michaelsson et al. (14). The modification that we used in this study accounted for both the number and size of acne lesions. The numbers of comedones, papules, pustules, nodules, and cysts on each side of the face were recorded. Each type of lesions was given a severity index as follows: 0.5 for comedo, 1 for papule (1–5 mm), 2 for pustule, 3 for nodule (>5 mm), and 4 for inflammatory cyst. Besides, scar type (pitted, atrophic, or hypertrophic) and pore size (small vellus or large sebaceous follicle) were documented. Fluorescence intensity of the half-face irradiated with blue light under Wood's light examination in a dark room was documented before and at the end of the treatment and was rated as negative, weak, moderate, or intense (15). All above-mentioned evaluations were assessed by two dermatologists unaware of the status of treatment.

#### Statistical analysis

We used the paired-samples *t*-test to assess the therapeutic effectiveness of blue light after two, four, and eight sessions of treatment. The one-way ANOVA was used to analyze the relation between pretreatment fluorescence intensity and the responsiveness to phototherapy, and the correlation between the therapeutic effectiveness and the fluorescence intensity change. Besides, Fisher's exact test was used to determine if gender, scar type, or pore size could be used as a predictor for therapeutic effectiveness.

## Results

#### Patient characteristics

Twenty-eight (10 males and 18 females) patients out of 31 completed the study. The mean age was 20.79 ± 3.96 years (range, 15–32 years). Their clinical characteristics are presented in Table 1. One patient dropped out after two sessions of irradiation and the other two dropped out after four sessions because of unsatisfactory results as claimed by the patients themselves.

#### Acne efficacy

Compared with the non-irradiation side, phototherapy with eight sessions of blue light was effective in the treatment of acne ( $P < 0.001$ ). Significant improve-

Table 1. Clinical characteristics of 28 patients with acne

Characteristic	Patient no. (%)
Gender	
Female	20 (71)
Male	8 (29)
Age categories (years)	
<20	12 (42.8)
20–30	15 (53.6)
>30	1 (3.6)
Severity (score)	
40.0	2 (7.1)
40.5–60.0	6 (21.6)
60.5–80.0	7 (25.0)
80.5–100.0	10 (35.7)
100.5–120.0	2 (7.1)
>120.0	1 (3.6)
Scar type (major)	
None	6 (21.4)
Pitted scar	8 (28.6)
Atrophic scar	12 (42.8)
Hypertrophic scar	2 (7.2)
Pore size	
Small	18 (64.3)
Large	10 (35.7)
Pretreatment fluorescence intensity	
Negative	0 (0.0)
Weak	11 (39.3)
Moderate	14 (50.0)
Intense	3 (10.7)

ment was first noted after four sessions of irradiation ( $P = 0.009$ ). The mean overall percentage improvement is shown in Fig. 1a. After eight sessions of blue light irradiation, the mean percentage improvement was 52%. Acne exacerbation was found in four patients (14.3%). These patients had more severe acne when first evaluated. To further analyze the effect of blue light irradiation on differently weighted acne lesions in all 28 patients, three groups were arbitrarily divided, including comedones, papulopustules, and nodulocysts. Compared with the mean percentage improvement in the non-irradiation site, the papulopustular group showed significant reduction in severity ( $P < 0.001$ ). However, the nodulocystic group tended to worsen ( $P = 0.026$ ), as depicted in Fig. 1b. Two patients showed further improvement, and exacerbation was noted in three patients at 1-month follow up. Gender ( $P = 0.471$ ), scar type ( $P$ -value of pitted, atrophic, and hypertrophic type were 0.688, 0.572, and 0.802, respectively) and pore size ( $P = 0.755$ ) cannot be used as predictive factors of therapeutic effectiveness.

#### Fluorescence intensity study

There was no correlation between pretreatment fluorescence intensity and therapeutic effectiveness ( $P = 0.656$ ). Moreover, therapeutic effectiveness was not related to fluorescence intensity change ( $P = 0.812$ ).

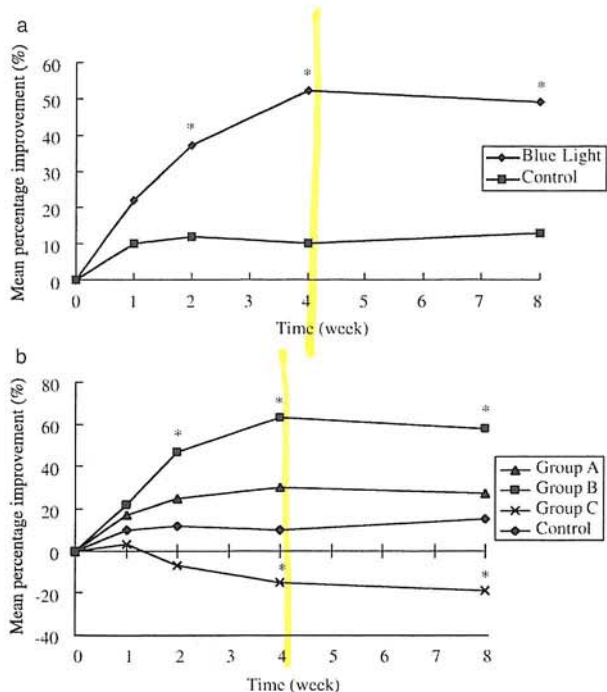


Fig. 1. Mean percentage improvement of overall acne severity (a) and in arbitrarily divided groups (Group A, comedonal group; Group B, papulopustular group, and Group C, nodulocystic group) (b) after two, four, and eight sessions of blue light irradiation and 1-month follow up ( $*P < 0.05$  compared with the non-irradiation control group).

## Discussion

The pathogenesis of acne is not fully understood. It appears to be a multifactorial process involving a high sebum secretion rate with a relative decrease in the level of linoleic acid, follicular hypercornification, overgrowth of *P. acnes*, and inflammation (2).

Bornmer (16), in 1927, first described the punctate orange-red fluorescence on the face using Wood's light examination. Later, Cornelius and Ludwig (17) demonstrated that a strain of *P. acnes*, which produced coproporphyrin III, accounted for the orange-red fluorescence seen under Wood's light. More recently, Lee et al. (18) examined several strains of *P. acnes* and *P. granulosum* and showed that both species synthesized coproporphyrin III. According to the results of McGinley et al. (15), the fluorescence intensity was proportional to *P. acnes* colony density (19).

*In vitro*, *P. acnes* was inactivated by cytotoxic singlet oxygen generated from coproporphyrin in *P. acnes* on irradiation with Argon laser (13). In 1990, Meffert et al. (19) reported that both acne and seborrhea improved markedly with a blue light-type high-pressure lamp after 10 irradiations, with a cumulative dose of  $325 \text{ J/cm}^2$ . Papageorgiou et al.

(20) chose an irradiation regimen with a lower irradiation dose each time but more sessions of irradiation, to a total dose of  $320 \text{ J/cm}^2$ , and demonstrated 45% and 63% improvement in comedones and inflammatory lesions, respectively. In our study, a 52% mean improvement was achieved after a total blue light irradiation dose of  $320 \text{ J/cm}^2$ .

In addition, our results indicated that papulopustular lesions responded to blue light irradiation better than either comedones or nodulocysts. The latter even seemed to be worsening after blue light irradiation. Increased severity in nodulocystic group could be because of exacerbation of lesions in the group *per se* or group shift of lesions from comedones or papulopustules. When patients' photographs were retrospectively reviewed, most nodulocystic lesions persisted or became worsen after irradiation. Only occasionally would papulopustular lesions progress to nodulocysts. In other words, acne patients without nodulocysts are better candidates for blue light treatment.

Fluorescence under Wood's light had been used as an indicator of the quantity of *P. acnes* (21, 22). After antibiotic treatment, fluorescence diminishes greatly because of the suppression of *P. acnes*. Meffert et al. (19) measured the amount of coproporphyrin extracted from comedones in five patients before and after blue light irradiation and found a correlation between a change in the amount of coproporphyrin and therapeutic responsiveness ( $r = 0.8$ ). However, Ammad et al. (23) found that *P. acnes* colony counts failed to show a significant decrease at the end of blue light phototherapy and remained almost constant. In our observation, pretreatment fluorescence intensity was not correlated with the responsiveness to blue light phototherapy. Moreover, the therapeutic effectiveness was not related to fluorescence intensity change. These two findings suggest that blue light has as yet unknown effects in acne treatment in addition to killing *P. acnes*.

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Accepted for publication 09 June 2004

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