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PHOTOTHERAPY FOR MILD TO MODERATE ACNE VULGARIS WITH PORTABLE BLUE AND RED LED

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In this paper, we studied portable blue and red light-emitting-diode (LED) light sources in phototherapy for mild to moderate acne vulgaris to evaluate the efficacy and tolerance of patients. Patients, randomly divided into blue and red groups, received either blue or red LED phototherapy twice a week for four weeks. After complete treatment, the number of lesions reduced by 71.4% in the blue group, in contrast to 19.5% in the red group. No obvious side effects were observed during and one month after the treatment, except for some mild dryness mentioned by several patients.

Keywords: Acne vulgaris; light emitting diode; phototherapy; portable light sources.

1. Introduction

Acne vulgaris, consisting of noninflammatory (comedo) and inflammatory (papule and pustule) lesions, is one of the most common dermatological disorders among juveniles, of which 80% are suffering from the physical, social, psychological, and emotional inconveniencies.[1,2] Presently, there are two major causes of acne vulgaris: overacting sebum secretion[3] and *Propionibacterium acnes* (*P. acnes* is a Gram-positive anaerobic bacterium).[4] Treatment with antibiotics or isotretinoin, either topical or systemic, is proven to be effective.[5] However, there are still side effects, such as drug-resistance,[6,7] depression,[8] and time-costing.[9] Novel safe and effective therapies are in demand to be introduced into clinical practice.

Phototherapy has been one of the most promising solutions to the defects listed above. *P. acnes*, which are anaerobic, produce endogenous porphyrins, such as Protoporphyrin IX and Coproporphyrin III, with several absorption peaks.[10,11] Light, especially blue light around 415 nm (peak of the Soret band) and red light around 630 nm (a much lower peak of Q bands), activates endogenous porphyrins to produce reactive oxygen series (the singlet-oxygen) and reactive free radicals. Those endogenous chemicals produced by such so-called "photodynamic effects"[12] are thought to damage lipid walls of *P. acnes*, which is lethal to the bacteria.[13−15] Besides certain effect on *P. acnes*, red light is proven to be effective to scarring process based on the mechanism of stimulating fibroblasts.[16−18] Since the applications of various

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light sources, phototherapy is accepted as additional, sometimes even major clinical practice in the acne treatment.[11,15]

Several types of light sources, including fluorescence, halogen, xenon, and tungsten lamps and recently lasers, are accepted by hospitals as routine treating methods or undergoing clinical trials. Sigurdsson *et al.* had performed clinical trials on patients with acnes using fluorescent lamps of full spectrum, green, and violet, and found moderate improvements in acne.[19] In 2002, Kawada *et al.* performed an open study of an enhanced narrow-band (407−420 nm) blue light source using metal halide lamp, as blue light phototherapy for acne vulgaris,[20] in which 64% reduction of lesions was observed. Berstain and his colleagues found that low-energy, double pass 1,450 nm laser treatment with a larger 12 mm-diameter spot size effectively reduced acne counts.[21] There are also other light sources used in the acne treatment trials, such as IPL (intense pulsed light) devices,[22−24] KTP (potassium titanyl phosphate) lasers[25,26] (532 nm), PDLs[27,28] (pulsed dye laser, 585−595 nm), etc. Significant improvements to various acne patients have been observed in the treatment using these light devices.[29]

However, these applications are limited by the damaging spectrum (ultraviolet band), size, and price. Novel technique of light emitting diode (LED) was then applied as light sources due to some innate advantages: low energy consumption, improved robustness, small size, and relatively low price compared to other lasers or lamps. Various LED devices targeting acne vulgaris emerged and were introduced into clinical practices. Currently, most of these LED devices, with large illuminating area covering whole face, are only equipped in hospitals to conduct clinical trials, while the cost for each session of treatment is consequently high.

Here, we performed the study of directly comparing portable blue and red LED respectively, to treat patients with mild to moderate acnes to evaluate the efficacy and the tolerance of patients. It would make acne treatment more convenient and less costly.

2. Patients

Patients were recruited by advertising the experiment publicly, and then divided into blue and red groups randomly, equal for each group. Before the recruitment, they were all informed of the necessary knowledge about the treatment of acne and signed the informed consent after confirmation of the treatment. The study protocol was approved by the ethics committee of Institutes of Biomedical Sciences of Fudan University. Patients aged between 18 to 40 years old and met the requirements of the experiment, with mild to moderate acne lesions. Twenty patients (6 males and 14 females) eventually completed the study throughout one-month treatment and one-month follow-ups. Exclusion criteria were pregnancy, lactation, history of allergic to sunlight or any other photosensitizer, oral contraceptive medication during the past six months, systemic disease with complications with dermatological diseases, systemic and/or topical antibiotic treatment during the past two weeks, and treatment of other medication against acne vulgaris during the past four weeks.

3. Materials and Methods

3.1. *Materials*

The light sources used in this study were blue and red LED portable devices (Fig. 1), developed by Rainbow Communications Corp. (CA, USA). The blue LED light source emits 405 ± 10 nm blue light at the power of 30 mW/cm^2 (at the distance of 2 cm away from the face), with the illumination area of about 10 cm^2. It is composed of 30 blue LED lamps in the array of hexagon. The red LED light source is similar to the blue portable device, except for the wavelength and power, which are 630 ± 10 nm and 48 mW/cm^2, respectively.

Eucerin Cleanse Gel (Eucerin, Germany) was used to cleanse face before exposure to light sources, in order to decrease the reflection and scattering caused by sebum which might reduce the effect of light sources. Protective glasses were used to protect the eyes from the damaging of intense light. They can block more than 95% of light around 415 nm or 630 nm for blue or red LED phototherapy, respectively.

Photographs of patients' faces were captured by the camera of Canon IXUS 90, under the mode of macrophotography and nonflashing. DermaSpectrometer (Cortex Technology, Hadsund, Denmark) was used to measure the facial hemoglobin and melanin indices to evaluate if there was any change in the skin pigmentation caused by the treatment.

(a) (b)

Fig. 1. Portable LED light sources for acne vulgaris treatment. (a) Blue LED light source, wavelength: 405 ± 10 nm. (b) Red LED light source, wavelength: 630 ± 10 nm.

3.2. *Procedures*

Patients were asked not to put up make-ups before treatment. After cleansing of face, each patient was photographed in the front, left, and right areas of face. Photographs were recorded to evaluate the acne lesions and as the original archives, which were confidential and will not be public without the informed consent of patients.

Before the first session, researchers taught patients how to use the device correctly. After wearing the protective glasses, patients held the light sources to illuminate different facial areas moving in the repeating sequence of forehead, left cheek, chin, right cheek, and T-shape area (nose). It took about 10 s for each area, and 20 min for one session. In each session, there were about 20 cycles of illumination and the corresponding light doses received in each session were 7.2 J/cm^2 and 11.52 J/cm^2. We performed the treatment twice a week, with an interval of two days, for four weeks as a complete treatment.

Prior to each session in the red group and after the last session, we used the DermaSpectrometer device to measure the facial hemoglobin and melanin indices to evaluate the skin pigmentation to find out if there was any change to face skin color. Each time, before the administration of therapy we evaluated at the same position, the center of forehead, to eliminate the bias.

One month after the completion of the last session, we conducted a follow-up for each patient through phone call to collect information of progress for acne lesions and to see if there were any long-term adverse events.

3.3. *Lesion counting*

Photographs taken as above were evaluated by skilled observer to count lesions in different areas of face, which were forehead, left and right cheeks, chin, and nose. Inflammatory lesions were divided into papules and pustules. All evaluations were conducted by one observer blindly to decrease random errors.

3.4. *Evaluation*

Equation (1) below was used to calculate the percentage of lesion changes. For each patient, the "inflammatory lesions pretreatment" stands for the number of inflammatory lesions counted the first time before treatment; the "inflammatory lesions post-session" means the number of inflammatory lesions counted after the eighth session. All patients were grouped into five classes[12]: full recovery (reduction over 90%, including 90%), significant improvement (reduction from 60% to 90%, including 60%, excluding 90%), moderate improvement (reduction from 40% to 60%, including 40%, excluding 60%), mild improvement (reduction from 20% to 40%, including 20%, excluding 40%), and non-improvement or aggravation (below 20%, excluding 20%). Efficacy is addition of full recovery, significant improvement, and moderate improvement.

$$\text{Average reduction} = \frac{\text{Inflammatory lesions pretreatment} - \text{Inflammatory lesions post-session}}{\text{Inflammatory lesions pre-session}} \times 100\%. \quad (1)$$

Subjective evaluation was based on the observations of face skin and communications between the patient and researcher (for the follow-ups). The patients were questioned about the side effects (erythema, pain, hyperpigmentation, dryness, etc.).

3.5. *Statistical analysis*

Statistical Package for Social Sciences (SPSS/PC+) program (Version 15.0 for Windows) was used to analyze the statistics of the result. Average reductions of each session were compared using paired t-test to find whether there was any significant difference between the pretreatment and last sessions. It was of statistical significance when P value was less than 0.05 ($P < 0.05$).

4. Results

4.1. *Patient characteristics*

Twenty patients, 10 for each group, have completed the full session of the treatment. In the blue therapy group there were 4 males and 6 females, while there were 2 males and 8 females in the red therapy group. They were scaled from mild to moderate level of acne vulgaris in GAGS[30] (Global Acne Grading System), with skin type ranging from III to IV. Patients in blue group aged from 20 to 28 years old, averaging 24.4 years old, with duration of acne disease history ranging from four months to six years, averaging three years. Patients in red group aged from 19 to 27 years old, averaging 22.8 years old, with duration of acne disease history ranging from four months to 10 years.

4.2. *Clinical efficacy*

We analyzed the photograph records of patient's face and counted the inflammatory lesions (papules and pustules) in different areas (forehead, right and left cheeks, chin, and nose). The calculation of papule and pustule numbers revealed the improvement or deterioration of acne (see Figs. 2 and 3).

For blue group, the average number of acne lesions dropped from 19.2 to 5.5 after eight sessions of treatment. P value was less than 0.05 when comparing number of lesions of pretreatment and post-treatment using paired t-test in SPSS. As shown in the graphs, the mean total number of lesions of patients declined significantly during observation in this group. Compared to pretreatment, there was more than 70% (71.35%) reduction of inflammatory lesions. According to the classification of improvement, there were 2 patients fully recovered, 5 of significant improvement, 1 of moderate improvement, 1 of mild improvement,

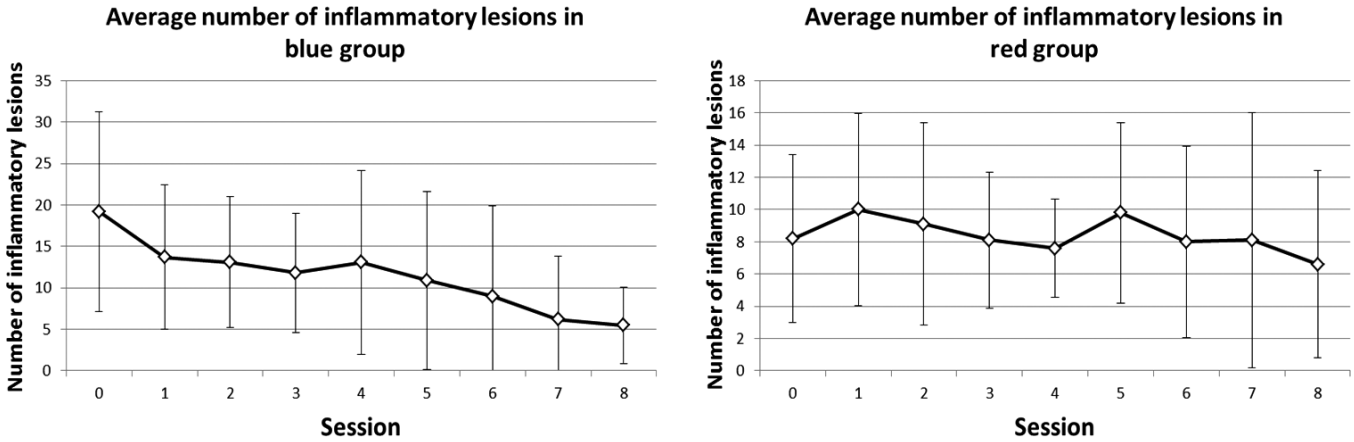

Fig. 2. Average number of inflammatory lesions in blue (left) and red (right) therapy groups. In the left blue group, the number of inflammatory lesions drops from 19.2 down to 5.5 significantly; as a contrary, the number in the red group changed from 8.2 to 6.6 with only 19.51% reduction. There is no significance between pretreatment and post-treatment in the red group as the P value is more than 0.05, whereas the P value is much less than 0.05 in the blue group.

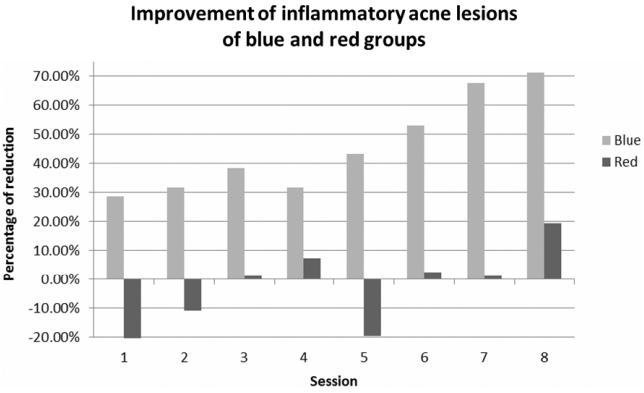

Fig. 3. The reduction of patient acne lesions in blue and red light phototherapy groups. The reduction in the blue group (compared to pretreatment) occurred gradually, from 28.65% after the first treatment session to 71.35% after the eighth session. However, the red curve shows that the percentage of reduction is around 0% with highest 19.51%, as well as increase in the number of lesions indicated by the bars below 0%.

and 1 of non-improvement or aggravation. As shown above, the efficacy is 80% ($= \frac{2+5+1}{10}$) during the one-month treatment with eight sessions for blue light phototherapy of portable LED light source. Figure 4 shows the typical improvement of acne inflammatory lesions in the forehead area of a female patient (with informed consent from patient).

For red group, no obvious improvement was observed during the treatment, and confirmed by the calculation later after analyzing recorded photograph files. P value was more than 0.05 indicating that there was no significant difference between pretreatment and post-treatment. As Figs. 2 and 3 showed, there were even increments of inflammatory lesions after the fifth session. Figure 4 shows the typical comparison of acne inflammatory lesions in the forehead area of a male patient (with informed consent from patient).

There were 4 patients of significant improvement, 1 of moderate improvement, 1 of mild improvement, and 4 for non-improvement or aggravation. As shown above, the efficacy is 60% ($= \frac{4+1+1}{10}$) during the one-month treatment with eight sessions for red light phototherapy of portable LED light source used in this study.

Follow-ups (recorded as questionnaires filled by researchers based on the phone call visit) were conducted one-month after the completion of treatment. A few patients reported that fresh new

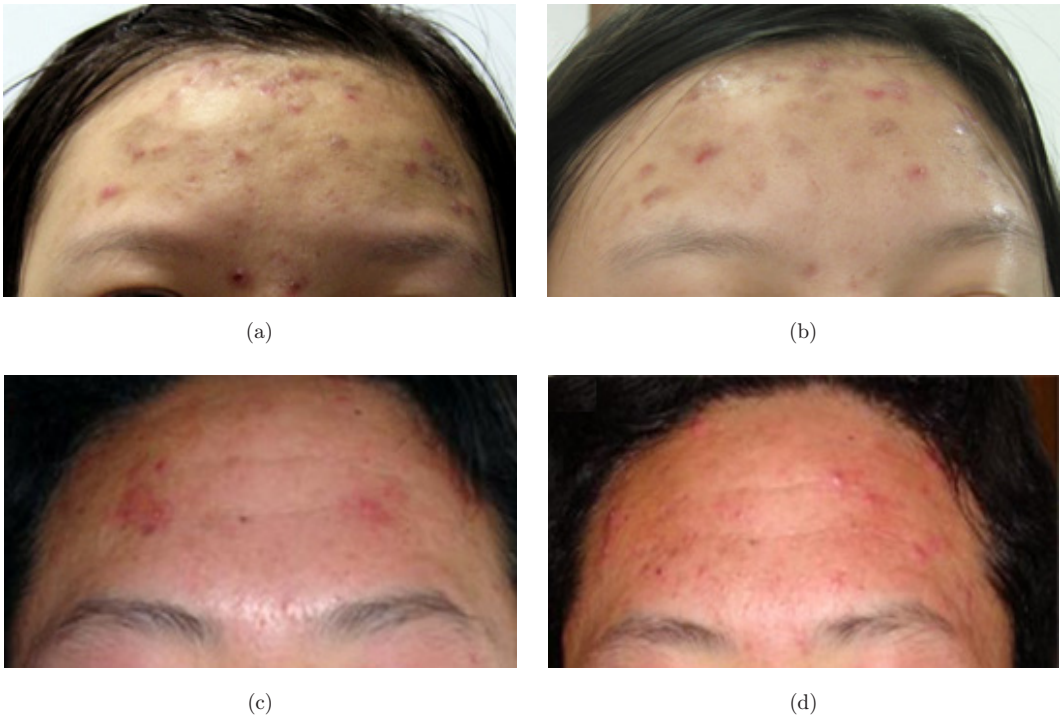

Fig. 4. Photographs of inflammatory lesions in the forehead. (a) and (b) show the contrast of lesions in a female patient's forehead between pretreatment and post-treatment (after the eighth session). The decrement of papules and pustules is significant, although leaving some scars as a healing symbol. (c) and (d) show a typical contrast of forehead acne lesions between pretreatment and post-treatment (after the eighth session). No significant improvement of acne could be found here, but with some aggravation.

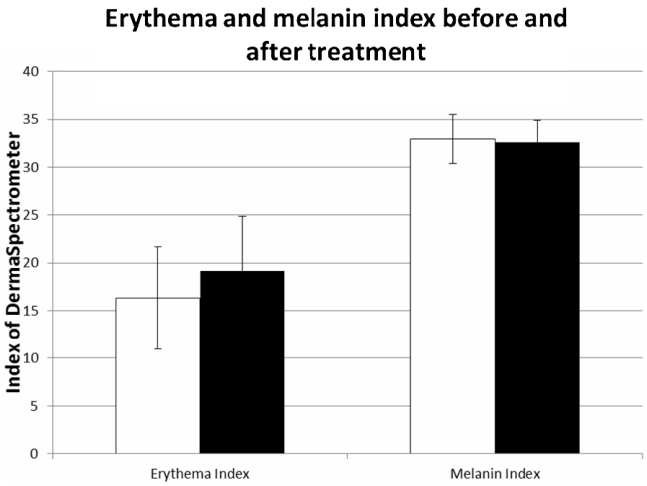

Fig. 5. Erythema and melanin indices measured by DermaSpectrometer in the red group. Hollow columns represent mean index of pretreatment; solid columns represent mean index of post-treatment. After statistical analysis using SPSS, there are no significant differences as P values are more than 0.05 (erythema index: 0.052, melanin index: 0.715).

acne lesions came out, while the total number of lesions decreased slightly.

4.3. *Side effects*

During each session of the treatment, we monitored any discomfort of patients, and found few reports about side effects. A few patients stated certain dryness of skin after exposure to light sources for 20-min session.

Previous studies have shown that there was no demonstrable significant change in erythema or melanin index after treatment in the blue light (415 nm) therapy using LED planar array.[31,32] However, other study has shown that melanin level decreased with a statistical significance after red light irradiation.[32] To examine the red light effect on the skin color, we examined the facial hemoglobin and melanin indices in the red group by DermaSpectrometer after each session to study if there was any erythema or tanning caused by the exposure to blue and red LED light. The result (shown in Fig. 5) demonstrated that there was no obvious change in skin color.

5. Discussion

Our study of blue and red light phototherapy of portable LED light sources has confirmed its effectiveness on reducing inflammatory lesions of acne vulgaris, especially in the blue light group. Blue light used in this study, the wavelength of which is the strongest peak of absorption by porphyrins (Protoporphyrin IX and Coproporphyrin III) produced by *P. acnes*, was proven here to be very effective in phototherapy. The results from blue light group are consistent with other research groups.[33] However, the red light was much less effective possibly due to the weak absorption by porphyrins, which is different from those results obtained in some previous studies.[18,34] Porphyrins have a much lower absorption peak in the Q bands. Therefore, red light with the same power as blue light in our case might have less ability to activate enough porphyrins to produce singlet-oxygen, to kill anaerobic *P. acnes*. Whereas considering the lower energy output per square centimeter (cm^2), which is approximately 3.6 J/cm^2 for each session of red phototherapy group, it is much lower than those for large systems, which could produce energy of 48 J/cm^2 or more per session.[18] This might explain why there is much less effect on the acne of red light phototherapy using our handheld device.

Our study demonstrated that red light with similar power as blue light (48 mW/cm^2 vs. 30 mW/cm^2) has much less efficacy than blue light. Nevertheless, red light with longer wavelength has instinct advantage in penetration, which could be several centimeters compared to millimeters of blue light. As a result, many researchers tried to apply red light to acne treatment, and therefore found positive outcomes.[32,34,35] However, during the process of our treatment, about 60% of patients receiving red light therapy became worse after the first two sessions until third session. There might be some stimulation mechanism of red light at lower intensity. Studies of exposure to red light of *Staphylococcus aureus* showed that the number of bacteria colony increased by 67.3% at 18 J/cm^2 of illumination; whereas decreased by 99.8% at 180 J/cm^2 of illumination.[36] Thereafter energy fluence could be one of the major factors influencing effect of phototherapy. More thorough investigations are required to illustrate how energy fluence affects the red light-based phototherapy for acne lesions.

Here we have studied a portable LED light source, which is much smaller and less costly than currently used illuminating systems (lasers, halogen lamps, and large LED matrix). Those devices, such

as Omnilux Blue[33] and Clearlight,[37] are applied as regular treatment in some hospitals and used to study treatment of acnes for several years. High power and large illumination area are advantageous, although more expensive and inconvenient for field use. Therefore, a portable, affordable, and easy-to-use LED light source studied in this experiment would be useful for acne patients to be treated in an effective and comfortable way. Further investigation is required to study this promising type of LED device. For instance, combination of blue and red light therapy (with the right energy fluence, respectively) might integrate both advantages of blue and red light, thus having probable synergistic effects. In addition, more patients should be recruited to reduce random errors.

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