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ORIGINAL RESEARCH REPORT

Clinical efficacy of home-use blue-light therapy for mild-to moderate acne

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Abstract

Introduction: Blue-light light-emitting diode (LED) therapy has become widely used for the treatment of inflammatory acne. In this study we evaluated the efficacy of a home use blue-light LED application in improving lesions and shortening their time to clearance. *Methods:* This was an IRB approved randomized self-control study. For each patient ($n = 30$), 2 similar lesions, one of each side of the face were chosen for treatment with either a blue-light LED hand-held or sham device. Treatments ($n = 4$) were conducted twice daily in the clinic and lesions were followed-up till resolution. Reduction in blemishes size and erythema and the overall improvement were evaluated by both the physician and the patients. Time to lesion resolution was recorded. *Results:* There was a significant difference in the response of lesions to the blue-light LED application as opposed to the placebo in terms of reduction in lesion size and lesion erythema as well as the improvement in the overall skin condition ($p < 0.025$). Signs of improvement were observed as early as post 2 treatments. Time to resolution was significantly shorter for the blue-light LED therapy. *Conclusion:* The results support the effectiveness of using blue-light LED therapy on a daily basis for better improvement and faster resolution of inflammatory acne lesions.

Key Words: *Acne vulgaris, blue-light therapy, home-use device*

Introduction

Acne vulgaris is one of the most common dermatologic conditions worldwide (1). Acne frequently persists for many decades with exacerbations and remissions throughout adolescence and adulthood making it potentially physically and emotionally harmful for patients (2). Mild-to moderate acne is generally treated with topical cleansers, astringents and benzoyl peroxide preparations while topical or systemic antibiotics are indicated for the more severe forms of acne. Recently, the proportion of acne patients with strains of *P. acnes* resistant to tetracycline, erythromycin or clindamycin has risen significantly and are now of major concern for those treating patients suffering from acne (3). Accordingly, light-based treatments have become, for many patients, an effective attractive alternative to traditional topical and oral medications (4).

The pathophysiology of acne results from the interaction of follicular hyperkeratinization, the presence of *P. acnes* in the follicular canal and an increase in sebum production (5). The acne lesion begins with follicles that become blocked by a plug which is the result of hyperproliferation of the keratinocytes lining the duct. These comedones can rapidly transform into inflamed lesions when a powerful immune response against the colonization of *P. acnes* is triggered.

P. acnes are porphyrins producing anaerobic bacteria. These porphyrins absorb light in the UV and visible spectrum (6). Once the bacteria are exposed to activating light of the proper wavelength, it becomes chemically active, inducing a photodynamic reaction which results in the destruction of *P. acnes.* This photosensitivity of the bacteria accounts for the improvement reported by most patients after exposure to sunlight during summer time (4). It has been shown that *in vitro* irradiation of *P. acnes* colonies with blue visible light leads to photo-excitation of the endogenous bacterial coproporphyrin III having an

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absorption spectrum peak at 415 nm, leading to singlet oxygen production, and eventually to bacterial destruction (7). *In vivo* clinical studies confirmed these results by showing clinical improvement of the skin and acne blemishes following phototherapy with visible light, and more specifically blue light (8–11).

The combination of technological advances in solid state source technology makes in-home light treatment feasible by over-simplifying the treatment process. We have recently reported on the efficacy and safety of self-applied, blue-light, light-emitting diode (LED) therapy in the treatment of mild to moderate inflammatory acne on the face (12–13). In the present study we evaluated the performance of a smaller size version of this technology designed specifically for the treatment of much smaller areas affected with mild to moderate acne.

Methods

This was a prospective, self control clinical study using the Tanda Zap (TZ) device (Pharos Life Corporation, a subsidiary of Syneron–Candela, Ontario, Canada). TZ is a 414 nm, blue, LED treatment that has been scientifically and clinically proven of killing the *P. acnes* bacteria involved in the pathogenesis of mild-to moderate acne (14). The devise will improve existing blemishes as well as prevent future outbreaks. It is indicated for the treatment of mild-to moderate inflammatory acne. Classification of acne based on an amended Burton acne grading scale (15) is given in Table I. The device is shown in Figure 1.

Table I. Types of acne.

Acne type	Description of condition
No acne	Total absence of acne and blemishes
Subclinical acne	Small number of blackheads and whiteheads; barely visible; first sign of blemish
Comedonal acne	Blackheads and whiteheads (slightly inflamed—may be red); blemishes are visible
Mild acne	• Several inflamed pimples—red in colour • Less than 20 whiteheads/blackheads or less than 15 inflammatory (red) lesions (pimples) or less than 30 total lesions (pimples) not all inflamed (red in appearance)
Moderate acne	• Many inflamed pimples (red in colour) and pustules (visible accumulation of pus in skin) • 20–100 whiteheads/blackheads or 15–50 inflammatory (red) lesions (pimples) or 30–125 total lesions (pimples) not all inflamed (red in appearance)
Severe nodular acne	• Inflamed pimples and pustules (visible accumulation of pus in skin) with a few deep nodular lesions (solid mass can be felt under skin—can sometimes be raised) • Greater than 5 cysts (solid mass of skin like a knot, can be raised or felt under the skin) or total white-heads/blackheads count greater than 100 or total inflammatory count greater than 50 or greater than 125 total lesions
Severe cystic acne	Many nodular cystic lesions (with signs of scarring)

Thirty patients at the Tennessee Clinical Research Center, Nashville, Tennessee, fulfilling the criteria of having mild to moderate acne (Table I) as well as satisfying all the inclusion/exclusions criteria (detailed in Table II) were included in the study after signing the informed consent form approved by the auspices of an institutional review board (IRB). Excluded from the study were patients who received treatment to their face with an investigational device or drug within 30 days and those who had excessive facial exposure to sunlight or artificial UV-light within one month prior the study. The subjects served as their own controls and all were treated by the Principal Investigator (PI) or his designated staff with both the active and sham devices. For each subject, 2 similar lesions (either papules or pustules of similar eruption status and age), one of each side of the face were identified by the physician and were randomly assigned to treatment of either the active or sham device. Upon pressing the start button, the treatment device provides a short one second vibration to signal the start of treatment, and then the LEDs are illuminated and vibration provided throughout the treatment cycle. The sham device has a completely similar look to the active device, but it does not deliver any therapeutic light and does not vibrate throughout the treatment cycle; it only provides a short vibration at the start and end of treatment to signal a complete cycle. The duration of each treatment is 2 minutes.

Table III provides information on the number of visits and of the different activities performed

Figure 1. Tanda Zap (pharos life corporation, a subsidiary of Syneron–Candela, Ontario, Canada).

Table II. Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Patients of either sex who have mild-to-moderate acne of the face	Patient is skin type V or VI
At least 12 years of age	Patient has severe acne vulgaris that requires prescription medications for this condition
Willing and able to comply with treatment	Patients that are using topical or systemic steroids or NSAID's (e.g. pain or skin conditions)
Willing and able to give consent, for subjects under 18 years of age the legal guardian is willing to give consent	Clinically infected lesions that require treatment with systemic antibiotics and or local antiseptics and or other treatment
Patient is skin type I–IV	Pregnant or nursing women
Female patients of childbearing potential must have a negative urine pregnancy test result at baseline and practice a reliable method of contraception throughout the study	Patients with a known history of poor compliance with medical treatment

throughout the study duration. Briefly, each subject received 4 treatments in 2 consecutive days (2 treatments per day spaced minimum of 2, to a maximum of 12 hours apart) and was followed for up to 10 days post the first treatment or until the lesions resolved. Visual examination and evaluation of the overall skin condition was performed by the physician and the patient at different time points as detailed in Table III. The two inflammatory lesions, similar in their appearance and severity were evaluated by both the physician and the subject pre and post each treatment in order to measure the difference over baseline in lesions treated with the active TZ vs. lesions that were treated with the sham. Lesions were evaluated using the following criteria: lesion size (not raised, slight, moderately or severely raised) and erythema (none, trace, moderate, severe). Additionally, both the physician and the patients rated each of the two lesions as worsened, no change, improved or resolved. Adverse events were monitored, and patients were photographed on each visit. Efficacy of TZ treatments was determined based on the comparison of degree and timing of lesions improvement post-treatment.

Data analysis was performed using the SPSS 16.0 statistical software. Where appropriate, ANOVA (repeated measures two-way analyses of variance); McNemar's non-parametric test for nominal data was used. The two blemishes were evaluated following each treatment to determine whether an improvement, as defined by blemish size and blemish redness, had occurred relative to the baseline assessment. For all analyses performed, the level of significance was 5% and the confidence interval, 95%.

Results

Thirty patients (28 females and 2 males, skin types I–IV with a mean age of 30 years) were included in the study. All patients had mild to moderate acne for a mean duration of 15 years (range 2–36 years).

We evaluated lesion response to treatment with the active vs. the sham device based on the change in lesion size, erythema and the degree of overall improvement as judged by the physician. Importantly, the distribution of lesions with regard to their degree of involvement was similar between the two sides of the face in order to allow an objective comparison in treatment response (refer to TX0 columns in Figures 2 and 3).Following two treatments, a significant difference was found in the degree of

Table III. Study visits flow chart.

Study visits flow chart	Day 1 Screen baseline TX 1	Day 1 TX 2	Day 2 TX 3	Day 2 TX 4	Day 10 *OR* until blemish resolves
Inclusion/exclusion criteria	X				
Written informed consent	X				
Medical history	X				
Concomitant medication query	X	X	X	X	X
Pregnancy test	X[1]				
Investigator evaluation	X	X	X	X	X
Subject evaluation	X	X	X	X	X
Treatment utilizing stated parameters	X	X	X	X	
Photography[1]	X	X	X	X	X
Subject questionnaire					X
Adverse event query	X	X	X	X	X
End of study					X

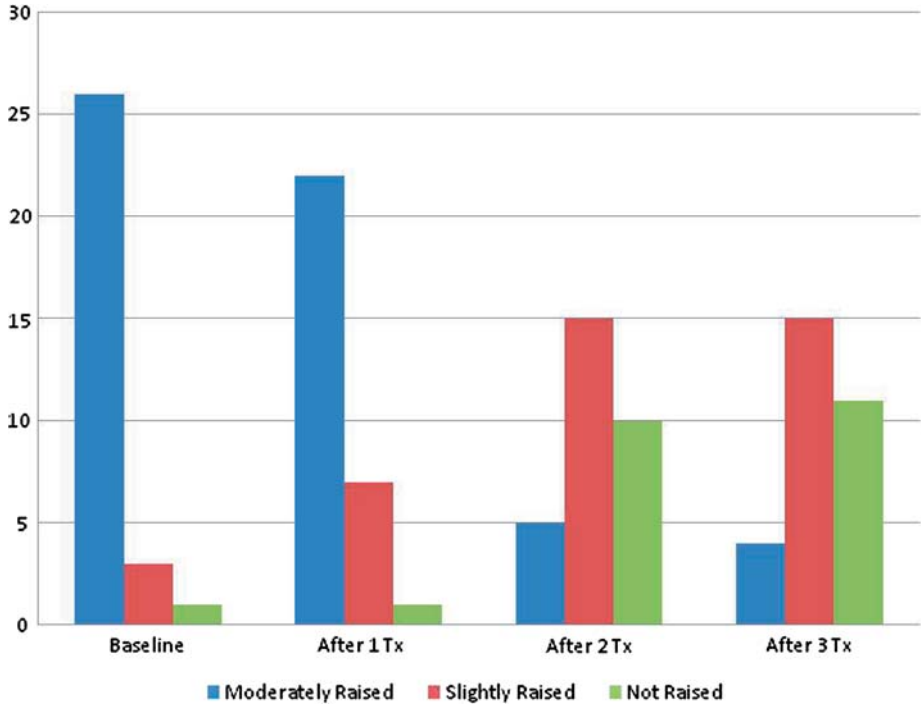

Figure 2. Stratification of inflammatory acne lesion size from baseline to post 3 treatments with the Tanda Zap device.

improvement in lesion size and erythema between those that were treated with the active unit versus lesions treated with the sham device ($X^2 = 5.79$; $p < 0.025$ and $X^2 = 4.08$; $p < 0.05$ for the reduction in blemish size and erythema, respectively). Furthermore, according to physician's assessment, the overall improvement in lesion condition following only 2 treatments was significantly different between the active and placebo units favouring the outcome of lesions treated with the active unit ($X^2 = 5.79$; $p < 0.025$). Importantly, as can be seen in Figures 2–4, for both the active and placebo treatments the reduction in lesion size and lesion erythema was progressive over time and became more notable following each treatment session. With the active device, as early as post the first treatment session, 19% of the moderately raised inflammatory lesions reduced their size while none of the sham treated lesions were

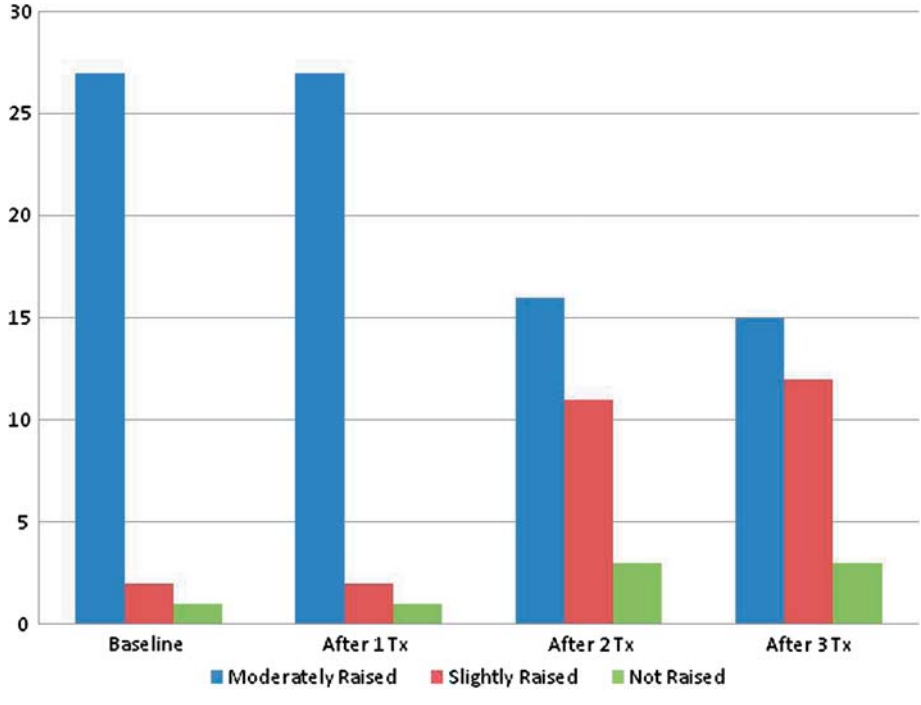

Figure 3. Stratification of inflammatory acne lesion size from baseline to post 3 treatments with the sham device.

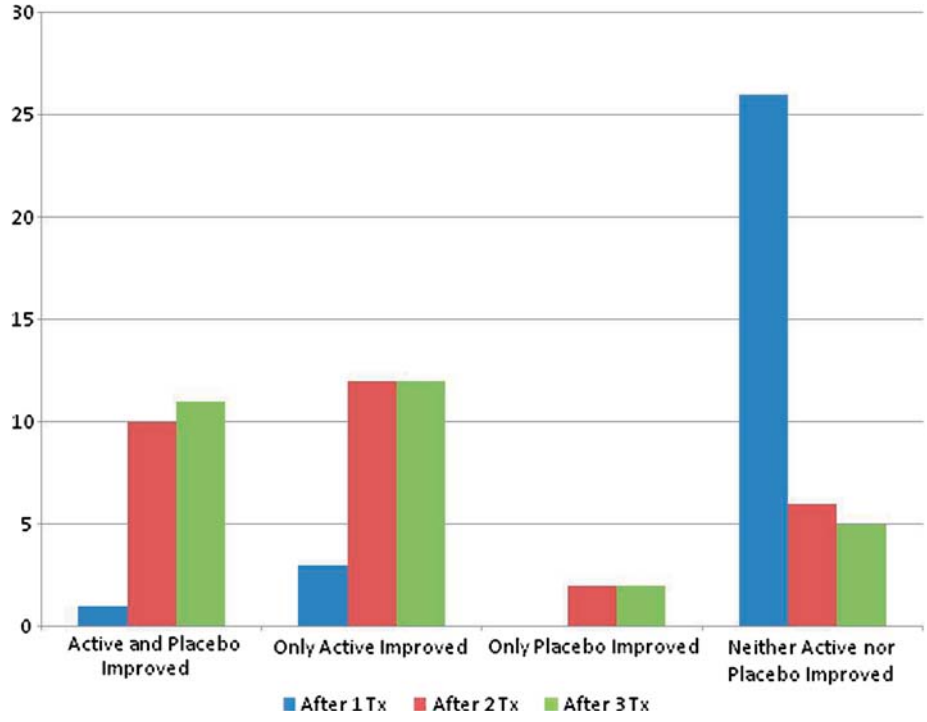

Figure 4. Degree of treatment response to the Tanda Zap device as compared to placebo following each treatment session (tx1–tx3) stratified by the number of inflammatory lesions improving and/or resolving.

improved. The best degree of improvement for both the active and placebo units was observed following two treatment sessions with 77% of the moderate and raised lesions improving or completely resolving if treated by the TZ device. With the sham device, the improvement was most noticeable post two treatments as well, but was significantly less remarkable as compared to the response to the active device with only 41% of the moderately raised lesions being improved or cleared at this time point of evaluation. Moreover, following three treatments, the number of lesions that reduces their size and erythema was significantly higher with the active device ($X^2 = 5.79$; $p < 0.025$ and $X^2 = 5.82$; $p < 0.025$ for the reduction in lesion size and erythema, respectively). By the end of all treatment sessions, the overall response to treatment with regard to lesion size was 76% with the TZ device compared to only 41% with the placebo. At this time point, we observed 37% complete clearance of lesions treated with the active unit as opposed to only 10% clearance achieved with the placebo (refer to TX3 columns in Figures 2 and 3). Consistent with

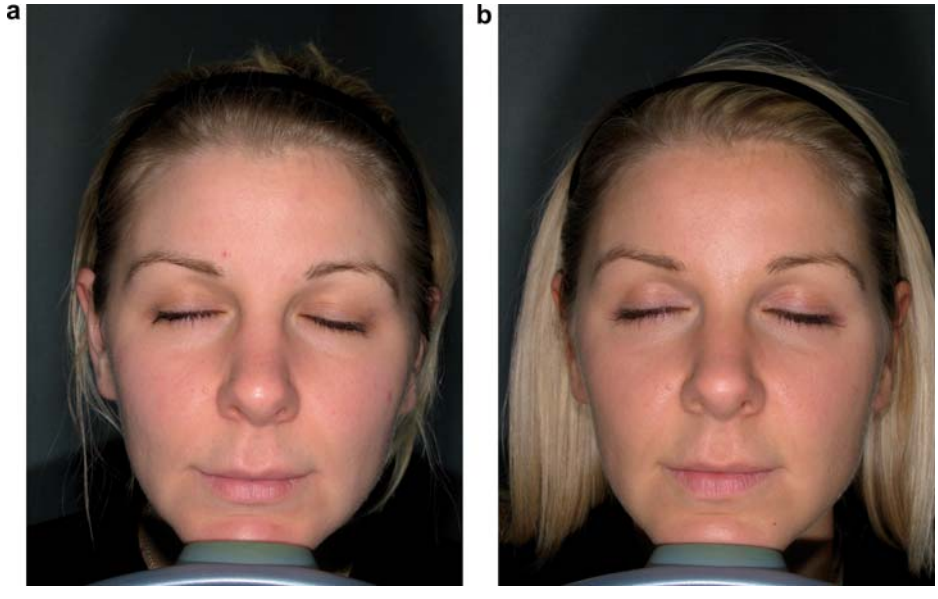

Figure 5. Clinical examples of 30-year-old female with skin type II treated with Tanda Zap (right side above brow) and sham (left side cheek); at baseline (A) and 10 days post four treatments (B).

these results, physician assessment of the overall improvement in the skin condition of the treated versus control was significantly graded higher than the improvement observed following only two treatments ($X^2 = 10.08$; $p < 0.001$). With regard to the timing of response, the first signs of improvement with the active device were noticed as early as few hours following the first session of treatment while the placebo treated blemishes showed no signs of improvement up to 24 hours posttreatment. Overall, the average time for improvement with the active device was only 29 hours compared with 45 hours for the placebo. Similarly, the average time to clearance was 99 hours for the active unit compared to 122 hours with the placebo device.

Consistent with the physician's evaluations, the proportion of patients observing an improvement in the lesion condition or their resolution was significantly higher for the active treated lesions as opposed to the placebo treated lesions ($X^2 = 4.35$; $p < 0.05$ and $X^2 = 4.50$; $p < 0.05$ for lesion improvement and resolution, respectively).

A clinical example is shown in Figure 5.

Discussion

This study demonstrates significant improvement of mild to moderate inflammatory acne using a home use LED device emitting at a wavelength of 414 nm with a twice-daily-treatment regimen administered for 2 days. The basic mechanism for phototherapy using LED sources lies within the endogenous coproporphyrins and protophorphyrins produced by the *P. acnes* metabolism leading to the destruction of the bacteria. Upon exposure to visible blue, red or green light, the endogenous porphyrins are excited and in the presence of oxygen generate reactive singlet oxygen species that damage the cell membranes of the bacteria (16,17). Since porphyrins are not normally present in skin, LED therapy has been shown to be safe and had recently received its FDA approval (18).

There are a number of studies supporting the efficacy of blue light LED therapy for treating inflammatory acne (9,19). In these studies the significant reduction in inflammatory acne lesions was achieved using the blue light LED source twice weekly. Self treatment with LED has many beneficial effects in addition to saving costs and time. Indeed, LED at a home-use setting is now widely spread (20). We and others have recently reported that self treatment with blue light LED light source applied daily effectively and safely reduced the number of acne lesions (12,13,21). In these reports, a similar but larger size version of the device being used here has been successfully applied by the patients to treat mild to moderate inflammatory acne lesions resulting in an overall improvement in their skin conditions. Moreover, patients found the device to be easy for use and friendly.

The technology being used here has been already proven for its usability, efficacy and safety (12,13). Our results demonstrate better and faster clearance of inflammatory acne lesions with the TZ device. To that end, two treatments sessions at least are needed, and the best results are obtained following four sessions.

Moreover, patients were in agreement with physicians' evaluations regarding treatment efficacy. Thus, the current study performed with the smaller version hand piece, designed specifically for the treatment of smaller areas, further support the efficacy of self-treatment blue light LED therapy in patients with mild to moderate acne. Importantly, in our study the first signs of improvement were noticed as early as following two treatment sessions and increased over time leading to a greater degree of acne resolution at an earlier time point.

Conclusion

Home use blue light LED therapy improved significantly the outcome of mild to moderate inflammatory acne lesions as demonstrated by the reduction in inflammatory lesion size and erythema, faster resolution and overall improvement in patients' skin condition and faster resolution of the lesions.

***Declaration of interests*:** Dr. Gold is a consultant to Pharos Life, a division of Syneron-Candela, speaks on their behalf and performs research.

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