A Randomised Controlled Study for the Treatment of Acne Vulgaris using High Intensity 414nm Solid State Diode Arrays

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A randomized controlled study for the treatment of acne vulgaris using high-intensity 414 nm solid state diode arrays

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Abstract

The treatment of acne vulgaris poses a challenge to the dermatologist, and the disease causes emotional anxiety for the patient. The treatment of acne vulgaris may be well-suited to home-use applications, where sufferers may be too embarrassed to seek medical treatment. This randomized controlled study is designed to quantify the effectiveness of using a blue light device in a therapy combined with proprietary creams, in the investigation of a self-treatment regimen. A total of 41 adults with mild-to-moderate facial inflammatory acne were recruited. The subjects were randomly assigned to combination blue light therapy (n = 26) or control (n = 15). Photography was used for qualitative assessment of lesion counts, at weeks 1, 2, 4, 8, and 12. All subjects in the treatment cohort achieved a reduction in their inflammatory lesion counts after 12 weeks. The mean inflammatory lesion counts reduced by 50.02% in the treatment cohort, and increased by 2.45% in the control cohort. The reduction in inflammatory lesions was typically observable at week-3, and maximal between weeks 8 and 12. The treatment is free of pain and side-effects. The blue light device offers a valuable alternative to antibiotics and potentially irritating topical treatments. Blue light phototherapy, using a narrow-band LED light source, appears to be a safe and effective additional therapy for mild to moderate acne.

Key Words: acne vulgaris, LED, light-emitting diodes, photorejuvenation, RCT

Introduction

Acne vulgaris is an exceedingly common chronic disease of the sebaceous gland and follicle, and accounts for over 30% of annual dermatology visits in the US (1). This condition hits adolescents at such a vulnerable time in their lives, undermining self-assurance and self-esteem. Not only can it cause disfigurement and permanent scarring, it can also have an adverse effect on psychological development, resulting in profound emotional scarring which may lead to social phobias, withdrawal, clinical depression, and suicide (2,3). It is the current consensus that acne is a multifactor disease which involves four primary events: follicular hyper cornification, increased sebum secretion, colonization by the gram-positive bacterium, Propionibacterium acnes (P. acnes), and inflammation (Figure 1) (4). The rise in antibiotic resistance threatens to reduce the future usefulness of the current mainstay of therapy. P. acnes plays a key role by producing lipases that hydrolyze triglycerides, and releasing its cytokines, which in turn trigger inflammatory reactions and alter infundibular keratinization (5).

Conventional topical therapies for acne vulgaris include the use of benzoyl peroxide, retinoids, topical antibiotics (i.e., clindamycin, erythromycin), salicylic acid, and glycolic acid. In addition, oral antibiotics and isotretinoin have been employed for systemic therapies (6,7). Oral antibiotics, while effective, are slow to produce an effect, and usually need to be taken regularly over an extended period of 6–8 months; moreover, antibiotic-resistant P. acnes have been documented since 1979. These treatments for acne also have a number of shortcomings, including the side-effects of socially unattractive dry skin, limited effectiveness, and the risk of benzoyl peroxide-containing preparations that may bleach hair and clothes and are often irritating to the skin. The side-effects of isotretinoin include xerosis of the skin and mucus membranes, as well as a number of more
severe conditions including visual disturbances and hypertriglyceridemia (8). There is also the danger of teratogenicity with isotretinoin therapy, which requires the use of contraception (9). In addition to the potential for long term scarring and disfigurement, acne vulgaris potentially carries with it significant psychosocial morbidity, including social withdrawal, clinical depression, and possible suicide (10–12). Other problems noted include impaired digestive functions due to the use of antibiotics (it requires treatment for several weeks to several months). Other treatments for acne vulgaris include stress management and ultraviolet light (9,13–15). Thus, there is a growing demand by patients for an effective, safe, and side-effect-free treatment for acne, as acne patients typically receive years of routine topical and systemic therapies. Patients have noted a decrease in their acne breakouts after sunlight exposure, with effectiveness up to 70% (4,16).

P. acnes produces porphyrins (17) which absorb light energy at the near ultraviolet (UV) and blue light spectra. Irradiation of P. acnes colonies with blue visible light leads to photoexcitation of bacterial porphyrins, singlet oxygen production, and eventually, bacterial destruction (18). In vitro, it has been shown that acne may be treated successfully with phototherapy, using blue visible light (19). The singlet oxygen leads to photoexcitation of bacterial porphyrins and singlet oxygen production, which destroys lipids in the cell wall of P. acnes (20). Photodynamic therapy using blue light has been shown to significantly reduce acne lesions in studies on mild to moderate, inflammatory and pustular acne, when irradiated for over 8 to 10 treatment sessions (13,21,22,23). This improvement corresponds with greater patient satisfaction, and has been found to be free of side-effects.

Papageorgiou et al. (24) investigated the effects of a combination blue and red light treatment delivered simultaneously, in a randomized study of 107 patients with mild to moderate acne. The results from a graded visual assessment displayed a 76% reduction in inflammatory lesions in the combination group, by daily, 15-minute treatment sessions spread over 12 weeks, and achieved a significant mean reduction in inflammatory lesions by 76%, compared with the 63% reduction achieved by blue light alone. Karu demonstrated that when Propionibacterium acnes was exposed to blue and red light simultaneously in vivo, there was a marked inhibition of cell activity compared to that seen when red and blue light were delivered independently (25). Goldberg and Russell produced a study evaluating the efficacy of a combination of 415 nm blue and 633 nm red light in the reduction of inflammatory lesions in both mild/moderate and severe acne patients, using a total of eight light treatments over a 4-week period, producing an 81% mean reduction at 12 weeks (26). Shalita et al. evaluated the use of a metal halide lamp with a wavelength of 405–420 nm for acne treatment, using ten-minute light exposures twice weekly. A total of 35 subjects with lesions on the face and back were treated over a 4-week period; 80% demonstrated a significant improvement of non-inflammatory, inflammatory, and total facial lesions, with a 70% mean decrease in inflammatory lesion-count two weeks after the last treatment (27). Blue light treatment also appears to have anti-inflammatory effects on keratinocytes by decreasing the cytokine-induced production of IL-1 alpha and ICAM-1 markers (28). Many clinical studies have shown the effectiveness of blue light on acne vulgaris. This study exploited the results of an in vitro study on the effects of wavelength and fluence on the
Materials and methods

This ethics committee-approved study recruited subjects aged between 16 and 45 years, with mild-to-moderate facial inflammatory acne defined according to the Leeds classification grading (29). Recruitment took place between December 2012 and January 2013, so that the confounding effects of summer sunlight could be avoided.

Washout periods for previous treatments were 8 weeks for oral antibiotics and topical treatments, 12 weeks for contraceptives containing cyproterone acetate, and 52 weeks for oral isotretinoin. Acne treatments were not allowed during the study. Subjects were instructed to cleanse their face daily with a facial cleanser containing glycolic, salicylic, and lactic acids, which was provided by the sponsor. Subjects in the treatment group were required to adopt the specified facial skin care regimen and avoid using any other facial skin care products, for the duration of the study. Continued use of non-comedogenic make-up, perfume, and body spray was allowed, but the use of non-study facial astringents, cleansers, creams, and lotions was prohibited. The pre-treatment and post-treatment creams contain salicylic, glycolic, and lactic acids, acting as a chemical peel. The post-treatment moisturizer contains niacin, which induces vasodilation and assists with skin regeneration. The user may experience temporary warmth, which subsides with additional applications. Treatment was performed every other day for 8 weeks, with a final assessment 4 weeks post-treatment.

Exclusion criteria were a history of photosensitivity and pregnancy or lactation. All subjects were screened prior to treatment, and a full medical history was recorded. All subjects gave informed written consent to inclusion in the trial. Subjects who had excessive facial exposure to sunlight or artificial UV-light within three months prior to the study were excluded.

Procedure

At recruitment, patients were randomized to either treatment or control by sequential numbers in sealed envelopes, in a 4/1 ratio. The allocations were concealed from assessors and patients throughout the study, and revealed only to the investigator (CA). After the first consultation, screened subjects in the treatment group watched a short video on how to use the device and creams, and were given a diary card, indicating treatment days and days for photographic assessment at the clinical office. The control group was given a diary card for photographic assessment dates, and a list of non-conformance medication and over the counter (OTC) products. All participants completed questionnaires at baseline, 3 months, and 6 months. Cohorts consisted of Caucasian, Asian, and mixed Afro-Caribbean ethnic groups.

The combined effect of daily pre-treatment and post-treatment creams with a light-emitting device provides more effective treatment than that achieved with the use of device or cream alone. The device is a hand-held LED light-emitting device with a rechargeable battery (the Dezac group Ltd, Cheltenham, UK). The device is designed to turn off after delivering a dose of 220 J, for effective and consistent treatment over a 12.5 cm² treatment area.

The photographic technique for capturing the full facial lesion for assessment was undertaken using digital photography, whereby the subject positioned their head towards 4 fixed positions within the clinical room, while sitting in the same position (Figure 2). Digital photography, with a Nikon 3100 digital camera, was used for lesion count assessment at baseline, and at 1, 2, 4, 8 and 12 weeks. The head position, angle, framing, exposure, and lighting conditions were standardized for all photographs. The overall assessment of the treatment, by the investigators and subjects, was recorded.

Grading acne by severity is a subjective method, evaluating the presence or absence of inflammation and dominant lesions. Previous studies have reported improvement in graded acne. However, in a pilot study, we found lesion counts to be of greater accuracy. In this study, the acne was quantified by lesion counts using custom software developed by the authors (Figure 3). The two assessors were blinded to the subjects’ cohort and assessment interval.
Results

Twenty six subjects were randomly assigned to the treatment cohort, and fifteen to the control cohort. Subjects in both groups had mild to moderate acne with a mean duration of 5.5 years. Three subjects withdrew from the study due to employment contracts. Two subjects were removed due to exposure to sunlight during the 12-week investigation.

Figure 4 presents the differential between the treatment and control cohorts. Mean lesion counts reduced by 50.08% \((p = 0.002)\) in the treatment cohort after 12 weeks, and increased in the control cohort by 2.45% \((p = 0.0029)\). The maximum clearance in the treatment cohort was 86%. Overall, every subject in the treatment cohort presented an improvement in their lesion count after 12 weeks. This improvement also correlated with an improvement in their social confidence and self-appearance.

The mean lesion counts of both cohorts over the course of the study is shown in Figure 5, illustrating a clear statistical difference between the cohorts. The average lesion counts show a dampened variation in the control group, due to the natural fluctuation in the acne disease condition.

Discussion

Antibiotic-resistant strains of \(P.\) acnes in patients treated for acne were first identified in 1979, and are now a major concern (30). The proportion of acne patients carrying strains of \(P.\) acnes resistant to tetracycline, erythromycin, or clindamycin rose from 34\% to 64\% between 1990 and 1997 in an urban population in the UK (31). Isotretinoin, a synthetic retinoid used to treat acne, has been associated with more serious adverse effects (32). An effective,
drug-free method of confronting this issue is presented in this study.

The basic mechanism for phototherapy using LED sources lies within the endogenous coproporphyrins and protoporphyrins, produced by *P. acnes* metabolism, leading to the destruction of the bacteria via damage to their cell membranes (33, 34). This safe and effective method allows treatment focused within the acne lesion, without an impact on internal organs as a consequence of oral medication.

There was a reduction in severity seen in the mean inflammatory lesion counts by 50.02% at the 12-week assessment. The initial reduction in mean inflammatory lesions was seen at around 3 weeks. This relatively quick response is in contrast to conventional treatments such as antibiotics, where 2–3 months are needed before benefits are seen.

The pre and post-treatment creams contained acidic compounds, which acted as a mild exfoliative peel, and 91% of the subjects recorded a smoother texture to their skin. Salicylic acid is a great peeling agent for improving skin texture, and is particularly effective in helping acne patients because it is comedolytic.

**Conclusion**

The optimum acne treatment would have long-lasting effectiveness in the control of active disease, improve acne scarring, have few local or systemic

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**Figure 4.** Lesion count at baseline and at 12 weeks, graphically showing all subjects in the treatment cohort presenting an improvement in the acne lesion counts.

**Figure 5.** Mean reduction of lesion counts in the assessment of the treatment cohort, compared to the control cohort.
side-effects, and is acceptable to patients. Ideally, visual improvement would be quicker than the results for current treatments available, i.e. antibiotics and OTC lotions.

The treatment with the blue light device is effective and well-tolerated, offering rapid, gentle, and convenient treatment of inflammatory acne, with the majority of subjects reporting that they were satisfied, very satisfied, or extremely satisfied with treatment. The blue light treatment is associated with significant reductions in the number, severity, and redness of flare-ups, and improvements in the skin’s overall appearance, as well as in clarity, radiance, tone, texture, and smoothness. In this study, we have been able to demonstrate that blue light therapy at 414 nm significantly reduces inflammatory acne lesions (Figure 6 & 7). Light absorption by target cells also induces changes in membrane permeability, leading to proton influx and dissipation of pH gradients across the cell membrane, thereby inhibiting the proliferation of P. acnes (13). The inhibition of proliferation, as well as the photodynamic destruction of P. acnes, could play a significant part in the response of inflamed acne skin to blue light.

The use of anti-comedone agents such as salicylic acid, in conjunction with blue light therapy to provide a practical yet effective therapy combination, is acceptable to today’s population of acne sufferers. This study is consistent with previous reports of blue light used in acne, and suggests that optimized blue light phototherapy deserves inclusion in the list of therapeutic options for patients with mild to moderate acne by healthcare professionals. Although the device works well as a monotherapy, its best suited to a combination therapy. After the completion of the study at 3 months and 6 months, all subjects under treatment recorded their responses within a questionnaire and noted that the severity of cyclic breakouts was noticeably reduced.

The psychological impact of acne is one that can dominate someone’s day-to-day life by affecting perceptions of themselves and how they perceive others to judge them, and result in spending their time either in actively treating and trying to conceal their acne or in thinking about their acne. The findings of a parallel study show that successful clinical treatment of acne can improve all of the negative aspects impacted by acne (35). This research also suggests that well-informed advice in terms of the possible psychological symptoms of acne, as well as physical symptoms, from both family and doctors before successful treatment, can also aid these negative psychological problems.

This study has demonstrated that combination therapy using creams and a non-thermal LED light source for acne treatment can improve the condition significantly.

Declaration of interest: Anna Harrison and Rebecca Whittall have no conflict of interest. Caerwyn Ash and Samantha Drew receive salary from The Dezac Group Ltd. The sponsors of this study had no role in the study design, data collection, data analysis, interpretation, or writing of the report.

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