

Comparative efficacy of filtered blue light (emitted from sunlight) and topical erythromycin solution in acne treatment: a randomized controlled clinical trial

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Abstract *Background* Acne vulgaris is one of the commonest skin conditions. The visible light has attracted attention as a new and safe therapeutic option, as some studies show more than 80% response to 420 nm phototherapy with a significant reduction in inflammatory acne lesions after only eight treatments.

Patients and methods We evaluated the use of blue light and topical erythromycin in 32 acne patients. The right-sided lesions were treated with erythromycin solution twice daily and the left ones were treated with irradiation of sunlight by a filter for 15 minutes once daily for 8 weeks and in another treatment group, the lesions in sides of the face were treated on reverse manner.

Results The difference between the treatment and control sides was not significant at week 4, and 8 ($p>.05$). After 12 weeks of starting the program, a mean improvement of 20% in lesion counts was achieved by the blue light phototherapy. In our study, a mean improvement of 46% in acne score was achieved with the blue light compared to 58% with topical erythromycin ($p>0.05$).

Conclusion We found that visible light phototherapy improved partially acne lesions and may be an appealing noninvasive alternative for the treatment of acne,

Key words

Acne, blue light, phototherapy.

Introduction

The mainstay of treatment of acne is the use of topical or systemic antibiotics. The rapid increase in the incidence of antibiotic resistance in the causative bacterium, *Propionibacterium acnes*, is causing great concern and there is a

pressing need for effective, non-antibiotic treatments. Available topical anti-acne treatments are slow and frequently irritating, so, the need for alternative therapies remains important.¹

The effects of blue light phototherapy on inflammatory acne lesions were recently investigated. Some studies show more than an 80% response to 420nm acne phototherapy with a significant reduction of 59-67% of inflammatory acne lesions after only eight

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treatments of 8-15 minutes.² *In vitro*, *P. acnes* has been inactivated by relative small doses (5 kJ/m²) of broadband near-UV radiation; this phenomenon was found to be oxygen dependent.³ The sensitivity was highest for the lowest wavelength used (320nm), decreasing continuously towards longer wavelengths but had a secondary maximum in the blue region at 415 nm. The latter corresponds to the absorption maximum of the porphyrins produced by *P. acnes*, which are very likely to act as chromophores. Acne often improves after exposure to sunlight artificially produced solar radiation. Blue light works by killing the acne-causing bacteria *P. acnes*, and is being used to treat inflammatory acne vulgaris that has not responded to other acne therapies.⁴ *P. acnes* produces porphyrins which absorb light energy at the near ultraviolet (UV) and blue light spectrum. Irradiation of *P. acnes* colonies with blue visible light leads to photoexcitation of bacterial porphyrins, singlet oxygen production and eventually bacterial destruction.³

In vivo, it has been shown that acne may be treated successfully with blue visible light phototherapy. Red light may have anti-inflammatory properties by influencing the release of cytokines from macrophages or other cells but its exact mode of action in the treatment of acne vulgaris is not yet fully understood.⁴ Recently, it has also been shown that irradiation of *P. acnes* with UVA and blue light, by affecting trans-membrane proton influx, induces intracellular pH alterations and bacterial damage.⁵

Macrophages exposed to 660nm low-level wavelengths release cytokines which stimulate fibroblast proliferation and the production of growth factors, thus influencing the inflammatory process, healing and wound repair.⁶ *In vitro* investigation revealed that

irradiation from this light source reduced the number of *P. acnes*, probably by combining antibacterial and anti-inflammatory action, which is nearly similar to topical antibiotic agents and a partially effective means of treating acne vulgaris of mild to moderate severity.

Our main objective is to compare the efficacy of filtered blue natural light in reducing acne severity score to topical standard solution of erythromycin in mild to moderate acne patients.

Patients and methods

This was an experimental, comparative clinical trial. 38 patients with mild to moderate acne of either sex and age ranging from 14 to 50 years (Fitzpatrick skin phototypes II-IV) attended the outpatient clinics at educational centers (Noor, Alzahra and Shahid Beheshti), and were recruited into the trial. They consented to participate in the study with full insight. None of the patients suffered from severe acne, an indication of systemic treatment. Exclusion criteria were: pregnancy, use of isotretinoin or other photosensitizer drugs e.g. thiazides, tetracyclines, benzodiazepines, use of any acne treatment other than that issued, or any intake of oral antibiotics, oral contraceptives, immigration, uncooperativeness and unwillingness to continue the treatment. All patients were otherwise healthy.

After the patients were recruited, a full medical and dermatological history was taken and a physical examination performed. Each patient's acne was assessed by a spot count of both inflamed and non-inflamed lesions.

Acne severity index (ASI) score was estimated by such formula: $0.25 \times \text{comedone number} + 1 \times \text{papule number} + 2 \times \text{pustule number} = \text{ASI score}$.

In one group of patients, after gently washing the face with *TCC soap (from the same manufacturer company), the right-sided lesions were treated with topical erythromycin 4% in 70% ethanol solution twice daily and the left-sided ones were treated with irradiation of sunlight by a filter of blue light (415nm) made by SAAIRAN Optics®. The portable light-weighted filter was touching the face for 15 minutes once daily at mid-day time, while another part of the face was covered with a dense black cloth. The tested light was blue (420-405nm) visible narrow band light with maximal conductivity of 40% of the filter and the band width of about 30nm.

Inflammatory and non-inflammatory acne lesions were counted at baseline and after each visit up to 4 weeks after cessation of the treatment period and the results were registered. The investigator assessed the global severity of acne at baseline and each study visit using acne severity index for grading. The patients were followed up to 12 weeks.

Criteria of improvement

Reduction up to 25% in ASI is regarded as poor improvement, 25-75% good improvement and above 75% regarded as marked improvement in our trial. An increase of more than 10% in ASI score compared to the baseline value was considered as the exacerbation of disease. A visual analog scale from 0=none to 5=severe was used for subjective assessment of the severity of disease.

Data were tested by t-test for changes in mean ASI score between two groups and by ANOVA variance analysis in each group in different time points.

Results

A total of 32 patients were registered in the study. There were 25 females and 7 males, with a mean age of 21.6 years. The baseline ASI score was on the filtered blue light side and erythromycin side was 17.5 ± 2.5 and 18 ± 1.2 , respectively ($p > 0.05$).

Six patients discontinued their treatment because of undesirable results and experience of deterioration and discomfort, though none of the patients showed any harmful direct side effects from filtered blue light phototherapy such as burns, pigmented macules, keratoses etc. One patient dropped out after two sessions of irradiation and the other three dropped out after four to five sessions because of unsatisfactory results as claimed by the patients themselves. Meanwhile, 2 patients refused from continuing the trial, as they did not like to use erythromycin due to undesirable smell and stinging sensation. So our study was completed by 32 remaining patients.

Exacerbation of acne was noted in three patients (3/32) on the side treated by blue light filter and in two patients (2/32) on the side treated by erythromycin at 1-month follow-up.

The percent improvement in lesion counts of the irradiated side was not significant compared to the control side ($p > .05$). Mean ASI changes in treatment group (irradiated) and control group (erythromycin) at baseline and 4-week, 8-week and 12 weeks were summarized in **Table 1**

By ANOVA analysis no significant differences were found between the groups at the baseline up to the end of study. There were not significant differences between the blue light and the erythromycin groups at all time points ($p > 0.05$). Meanwhile, gender ($p = 0.471$), could

Table 1 Changes in the acne severity index (ASI) in treatment group and control group at baseline and 4-week, 8-week and 12 weeks

	Treatment group (blue filtered light) n=32 Lesion, ASI median (range)	Control group(erythromycin solution) n=32 Lesion, ASI median (range)	P-value
Baseline	17.5 (12-23)	18 (12-24.5)	0.74
4 weeks	14 (10-20.5)	12.0 (10-13.5)	0.53
8 weeks	14.5 (9.5-20)	12.5 (9.5-14.5)	0.52
12 weeks	15 (10-19.5)	13 (10.5-16)	0.52
P value	0.43	0.20	

Data analysis (ANOVA Variance analysis test): Aiming for a significance level of 0.05 and a power of 80%.

Table 3 Prevalence of side effects in treatment group and control group during the treatment

Side effects	Treatment group (blue filtered light) n=32	Control group (erythromycin solution) n=32	P value
Exacerbation of lesions	3 (9%)	2 (6.3%)	>0.05
Drying effect	6(18%)	9(28%)	>0.05
Mild erythema and stinging	8(25%)	3(9%)	=0.03

T-paired test was used for comparison between groups

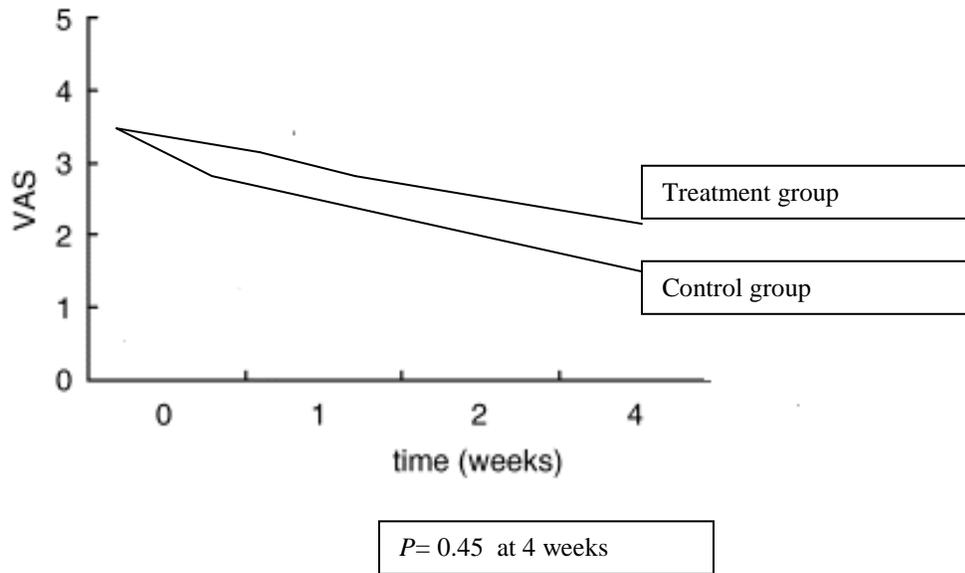


Figure 1 Visual analog scale of the treatment and control sides. $p < .005$ between the treatment and control sides. Visual analog scale (VAS) was measured by the subjects from 0 (none) to 5 (very severe).

not be used as predictive factor of therapeutic effectiveness.

Adverse reactions are summarized in **Table 2**. Except for erythema and stinging which were more common in irradiated side than erythromycin side, 25% vs. 9% ($p < 0.05$), the other side effects such as drying effect and

exacerbation of lesions were not significantly different in both sides ($p > 0.05$).

VAS decreased from 3.9 to 1.9 on the erythromycin side and from 3.9 to 2.4 on the light irradiated side, and the difference between them was not significant at week 4 ($p = 0.45$) [**Figure 1**].

About 50% of patients were highly satisfied with the treatment by erythromycin and only 39% with irradiation of light.

The recurrence as defined by increase of more than 20% in acne score after its reduction at the end of follow up was seen in 8 patients in blue light group and in 10 patients in erythromycin group and the result was not statistically significant (Mann-Whitney Test), ($p=0.41$).

Discussion

In a study by Morton *et al.*⁷ eight 10- or 20-minute treatments over 4 weeks with a narrowband blue light was found to be effective in reducing the number of inflamed lesions in subjects with mild to moderate acne. Some studies showed more than an 80% response to 420nm acne phototherapy with a significant reduction of 59-67% of inflammatory acne lesions after only eight treatments of 8-15 minutes.²

In our trial, the improvement achieved by the topical erythromycin was marginally superior to those of blue light, but the differences did not reach levels of statistical significance (with 95% confidence intervals). We conclude that phototherapy with blue light is partially effective and safe. In contrast to the red light that worsens the rosacea and causes skin hypersensitivity, blue light does not give rise to such side effects.⁸

Combination blue and red light therapy appears to have excellent potential in the treatment of mild to severe acne. Treatment appears to be both pain- and side effect-free.⁹

Optical treatments possess the potential to improve inflammatory acne on a short-term basis with the most consistent outcomes for photodynamic therapy [up to 68% improvement

with aminolevulinic acid (ALA), methylaminolevulinic acid (MAL) and red light]. IPL-assisted PDT seems to be superior to IPL alone. Only two trials compared optical vs. conventional treatments, and further studies are needed. Side-effects from optical treatments included pain, erythema, edema, crusting, hyperpigmentation, pustule eruptions and were more intense for treatments combined with ALA or MAL.

Conclusion

Evidence from this controlled clinical trial indicates a short-term efficacy from optical treatment for acne vulgaris.

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References

1. McGinley KJ, Webster GF, Leyden JJ. Facial follicular porphyrin fluorescence. Correlation with age and density of *Propionibacterium acnes*. *Br J Dermatol* 1980; **102**: 437-41.
2. Elman M, Slatkin M, Harth YJ. The effective treatment of acne vulgaris by a high-intensity narrow band 405-420nm light source. *Cosmet Ther* 2003; **5**: 111-7.
3. Kjeldstad B. Photoinactivation of *Propionibacterium acnes* by near ultraviolet light. *Z Naturforsch* 1984; **39**: 329-35.
4. Papageorgiou P, Katsambas A, Chu A. Phototherapy with blue (415 nm) and red (660 nm) light in the treatment of acne vulgaris. *Br J Dermatol* 2000; **142**: 973-8.

5. Breitbart H, Levinshal T, Cohen N *et al.* Changes in calcium transport in mammalian sperm mitochondria and plasma membranes irradiated at 633 nm (He-Ne laser). *J Photochem Photobiol* 1996; **34**: 117-21.
6. Iusim M, Kimchy J, Pillar T *et al.* Evaluation of the degree of effectiveness of Biobeam (low level narrow band light) on the treatment of skin ulcers and delayed post-operative wound healing. *Orthopedics* 1992; **15**: 1023-6.
7. Morton CA, Scholefield RD, Whitehurst C, Birch J. An open study to determine the efficacy of blue light in the treatment of mild to moderate acne. *J Dermatol Treat* 2005; **16**: 219-23.
8. Goldberg DJ, Russell BA. Combination blue (415 nm) and red (633 nm) LED phototherapy in the treatment of mild to severe acne vulgaris. *J Cosmet Laser Ther* 2006; **8**:71-5.
9. Haedersdal M, Togsverd-Bo K, Wulf HC. Evidence-based review of lasers, light sources and photodynamic therapy in the treatment of acne vulgaris. *J Eur Acad Dermatol Venereol* 2008; **22**: 267-78.