

Light Therapy in the Treatment of Acne Vulgaris

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BACKGROUND. Over the past decade, lasers and light-based systems have become a common modality to treat a wide variety of skin-related conditions, including acne vulgaris. In spite of the various oral and topical treatments available for the treatment of acne, many patients fail to respond adequately or may develop side effects. Therefore, there is a growing demand by patients for a fast, safe, and side-effect-free novel therapy.

OBJECTIVES. To address the role of light therapy in the armamentarium of treatments for acne vulgaris, to discuss photobiology aspects and biomedical optics, to review current technologies of laser/light-based devices, to review the clinical experience and results, and to outline clinical guidelines and treatment considerations.

RESULTS. Clinical trials show that 85% of the patients demonstrate a significant quantitative reduction in at least 50% of the lesions after four biweekly treatments. In approximately 20% of the cases, acne eradication may reach 90%. At 3 months after the last treatment, clearance is approximately 70% to 80%. The nonrespondent rate is 15% to 20%.

CONCLUSIONS. Laser and light-based therapy is a safe and effective modality for the treatment of mild to moderate inflammatory acne vulgaris. Amelioration of acne by light therapy, although comparable to the effects of oral antibiotics, offers faster resolution and fewer side effects and leads to patient satisfaction.

M. ELMAN, MD, AND J. LEBZELTER, PHD HAVE INDICATED NO SIGNIFICANT INTEREST WITH COMMERCIAL SUPPORTERS.

THE USE OF light, heat, and biostimulation has a long history in both oriental and Western medicine. Although the therapeutic benefits of light, heat, and biostimulation are generally known, it is only relatively recently that it has been used to any significant degree in medicine. Over the past decade, lasers and other light-based devices have become common modality to treat a wide variety of skin-related conditions, including acne vulgaris.^{1,2} Recent estimates suggest that 40-million American adolescence and 25-millions adults are affected by acne. Acne also accounts for more than 30% of all dermatologist visits each year.^{3,4}

In spite of the various oral and topical therapies available for the treatment of acne, many patients failed to respond adequately or developed unwanted adverse side effects.^{5,6} This therapeutic “vacuum” has created a large demand for a novel solution, particularly in patients for whom acne became a medical, social, and psychologic problem.

In order to address the ever-growing demand for fast, safe, and side-effect-free therapy, several aesthetic laser manufactures have recently begun launching light-based devices aimed to capture a niche in a large market that has been traditionally dominated by the pharmaceutical companies.⁷

Although for many years, dermatologists were aware of the favorable effect of sunlight on acne symptoms, it was unclear which wavelengths of light—ultraviolet, visible light, or a combination—are responsible for this effect. However, recent advancement in photomedicine and biomedical optics created new possibilities for the patient and the clinician alike.

Based on clinical experience gained in the last 5 years, lasers/light-based devices may offer an alternative to conventional acne modalities in selected patients, such as nonresponder or noncompliant patients, in antibiotic-resistance patients or even as a precursory therapy to Accutane regimen.

This review brings the latest update in the field of light therapy and acne and the role that light therapy plays in the armamentarium of treatments for acne. Pertaining to this review are the following topics: photobiological principles in acne, biomedical and photobiological considerations, the therapeutic meaning of acne by different wavelengths, and clinical experience and considerations of laser/light-based technology.

Photobiological Principles in Acne Treatment

A molecule that is absorbed in the skin is named chromophore. Each and every photobiological process starts in absorption of light energy by a selected chromophores. Every chromophore has a specific

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absorption spectrum of its own. After absorption, the chromophore is transformed from its stable state to the excited state. This unstable condition induces chemical reaction and a photoproduct. The biochemical changes cause reaction of the skin. In humans, the skin contains chromophores that are photodynamically active and photoinstable substances.⁸

The Gram-positive microaerophilic skin bacterium *Propionibacterium acnes* is implicated in the pathophysiology of acne vulgaris.⁹ As part of its normal metabolism process, *P. acnes* produce porphyrins, mainly protoporphyrin and coproporphyrin—photosensitizers.¹⁰ Photosensitizers are molecules that have the trait of absorbing light energy and using this energy to carry out chemical reactions in cells and the body tissues. Each photosensitizer has its proper wavelength of absorption, usually several, and a wavelength of emission. Excitation of the porphyrins by absorption of light causes the formation of singlet O₂ and reactive radicals.¹¹ Figure 1 describes schematically the process of *P. acnes* photoinactivation under light illumination conditions.

Porphyrins are a ubiquitous class of naturally occurring compounds containing the porphin structure of four pyrrole rings connected by methane bridges in a cyclic configuration, to which a variety of side chains

are attached, usually metallated, for example, with iron to form heme.¹² The basic structure of a porphyrin is shown in Figure 2.

In porphyrin-visible absorption spectra, the highly conjugated aromatic macrocycle shows intense absorption in the neighborhood of 400 nm; the highest peak of light absorption (and sensitizer activation) is called the “Soret Band” (Figure 3). It is usually located in the blue and ultraviolet range. Because the highest peak of absorption of porphyrin is at blue light (415 nm), some light source systems use this spectrum for the treatment of acne. Visible spectra of porphyrins also show several weaker absorptions (Q Bands) at longer wavelengths (450 to 700 nm).

The efficacy of *P. acnes* photoinactivation is determined by the rate of production of excited porphyrins molecules. In order to achieve maximum process efficacy, the controlled parameters in this complex photobiological process—concentration of photons, temperature and the wavelength of photons—can be technologically optimized. Most of

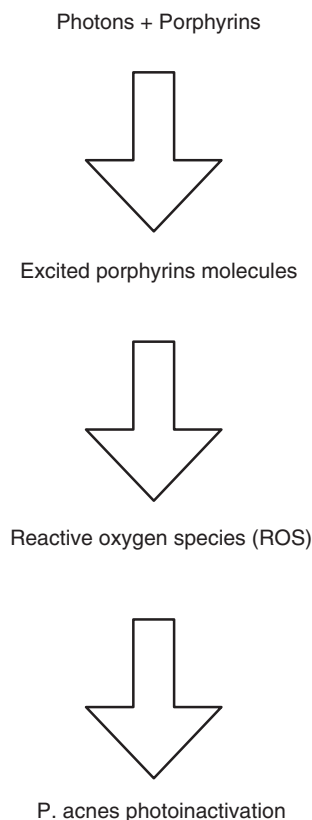


Figure 1. Schematic *P. acnes* photoinactivation chain of reactions.

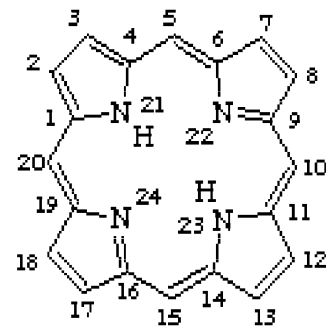


Figure 2. The basic structure of porphyrin.

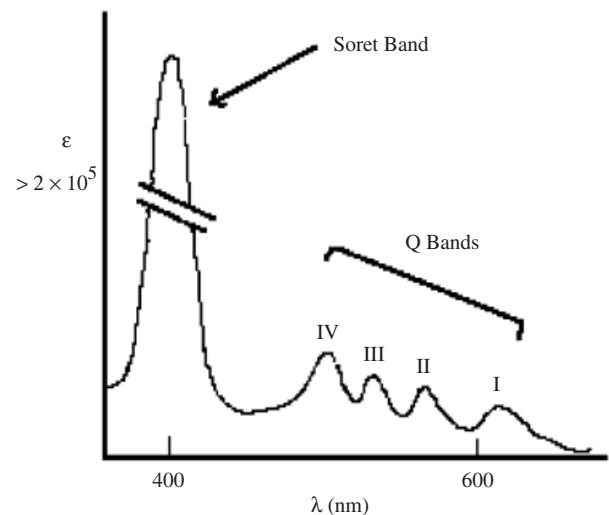


Figure 3. Typical UV-visible absorption spectrum of a porphyrin. Units ϵ = extinction coefficient, L/(m cm); λ = wavelength, nanometer.

the existing laser/light-based devices, however, are limited by one of the previously mentioned parameters, which may alter *P. acnes* photoinactivation efficiency. Table 1 shows the major factors that may influence *P. acnes* photoinactivation.

Lasers/Light-Based Technology for the Treatment of Acne

Over almost a century, many types of light sources were introduced in the hope to treat/improve acne symptoms. These light sources include fluorescent, halogen, xenon, tungsten lamps, and recently lasers. Table 2 depicts selected lasers and light sources for the treatment of acne.

Light-induced inactivation of dye-labeled bacteria by photodynamic reactions was pioneered by von-Tappeiner and Jodlbaurin in 1904.¹³ In 1924, Passow and Rimpau¹⁴ found a higher photodynamic inactivation rate in Gram-positive bacteria versus Gram-negative bacteria. The first light sources for the treatment of acne were conventional lamps where the output was defined by the use of filters. A drawback with this was that calculating the delivered light dose was difficult. High-intensity visible light phototherapy for acne was described by Meffert et al.,¹⁵ but they used a light source emitting not only visible light but also ultraviolet A (UVA) comprising up to 15% to 20% of the total irradiation dose. Sigurdsson et al.¹⁶ used Philips HPM-10,400 W combined with an

UVILEX 390-nm filter (Desag, Germany) that filters most but not all UVA harmful rays. The spectrum of their lamp peaked at 420 nm and had two other small peak of emission at 405 and 435 nm. Their apparatus emitted at 40 cm, 0.5 J/cm² of UVA, 20 J/cm² of violet/blue, and 5 J/cm² of green light.

Recently, a newly developed high-intensity, enhanced, narrow-band, blue-light source (CureLight) was introduced for the treatment of mild to moderate acne. This apparatus uses high-intensity, 400-W, enhanced blue light, a metal halide lamp, plus double UV-cut filters with the emitting peak of 407 to 420 nm, which produces 90 mW/cm² homogeneous illumination over an area of 20 × 20 cm². The system destroys the *P. acnes* bacteria in facial, back, and chest sebaceous glands by targeting the porphyrins in the bacteria. Last summer, the system has been cleared by the Food and Drug Administration to market for acne treatment.

Another light-based acne clearance system is Clear-Touch. The system is a broad-spectrum (430 to 1200 nm) flash lamp light source. The system uses the yellow and green bands (500 to 600 nm) to allow greater skin penetration (several mm) but has a lower extinction coefficient Q Band (Figure 3). Food and Drug Administration approval is pending.

While the previous two light-based systems target *P. acnes*, a secondary effect of acne, Smoothbeam diode laser targets the sebaceous glands. Although acne treatment, aimed at reducing the size of the sebaceous glands, has been quite successful with the drug Isotretinoin, the use of the drug is often limited because of many side effects. The Smoothbeam uses a 1450-nm wavelength to alter the sebaceous glands thermally at the sites of the acne lesions. Laser energy from the device is absorbed by the water in the upper papillary dermis where the sebaceous gland resides. The heat from the absorbed energy creates a thermal injury and alters the structure of the sebaceous glands.

Table 1. Factors Influencing *P. Acnes* Photoinactivation

Concentration of porphyrins—depends on acne lesion type
Concentration of photons
The wavelength of the photons emission
Temperature at which the chemical reaction is done

Table 2. Laser and Light-Based Devices for the Treatment of Acne

Light Source	Manufacturer	Model	Parameters	Target/Chromophore
Fluorescent lamps	Sylvania, Belgium	HF 885, Osram	415 nm 660-nm	<i>P. acnes</i> <i>P. acnes</i>
Full spectrum light	Philips	HPA 400 W	Visible and UVA	<i>P. acnes</i>
Green light	Philips	Thalium & Schott KV	470-nm filter	<i>P. acnes</i>
Violet light	Philips	HPM-10 & Desag UVILEX	390-nm filter	<i>P. acnes</i>
Blue metal halide lamp	CureLight	ClearLight	407 to 420 nm	<i>P. acnes</i>
Xenon flash lamp	Radiancy	ClearTouch	430 to 1200 nm	<i>P. acnes</i>
Lasers	Candela	Smoothbeam	1450 nm	Sebaceous gland
	Cynosure	PhotoGenica	595 nm	Oxyhemoglobin
	Cynosure	Unknown	800-nm+ICG*	Sebaceous gland

ICG = indocyanine green.

Nonpostular acne can be treated with the Photo-Genica V pulsed-dye laser. The device emits light of 595-nm wavelength that is absorbed by the oxyhemoglobin. The technology claims to improve the erythema that acne causes. However, the postular phase must be treated by conventional therapy before laser treatment. Food and Drug Administration clearance for acne is currently pending.

Some companies are also studying the application of photodynamic therapy (PDT) for the treatment of acne. PDT operates on a similar principal as laser and light-based treatment. Light energy is used to kill the *P. acnes* bacteria that cause skin eruptions. However, although other devices require expensive, high-power equipment to generate this light, PDT uses a lower power light source in which the effectiveness is amplified by the use of a topical agent. Currently, PDT is being used with 5-aminolevulinic acid, in conjunction with different light wavelengths. When delivered to target tissues, 5-aminolevulinic acid is taken up and converted into protoporphyrin IX, a potent photosensitizer, which can be then activated by an appropriate light source.

Biomedical and Photobiological Considerations

In the last 5 years, important technological advancements were introduced to the field of light therapy and acne; these include the following: (1) the use of a pulsed wave mode technology; (2) the ability to deposit heat energy to the acne lesion from a nonoptical, exogenous, energy source; and (3) the optimization of laser/light-based parameters such as wavelength, pulse width, and spot size.

Laser/light-based devices can emit light either continuously or in pulses. The nature of laser/light-based tissue interaction is usually different for continuous wave mode as compared with high-energy pulsed wave mode.¹⁷ In the continuous-wave mode, lasers/light-based systems work unremittingly and deliver a constant power, albeit low peak power. In contrast, in pulsed wave mode, the tissue exposure duration is short, and peak power is high. For example, for a 3.5 J/cm² pulsed wave light source with a 35-ms pulse width, the power rate is 100,000 mW/cm² compared with 10 mW/cm² in continuous-wave light source of the same wavelength. Thus, the pulsed-wave light source delivers 10,000 times more photons per second than the continuous wave source. However, although peak intensity (irradiance) is different, total energy (fluence) delivered to the tissue by both modes at a given time interval is the same.¹⁸

Temperature plays pivotal role in biological system reactions. For most of the chemical reactions, elevating the temperature by 10°C doubles the speed

of the reaction.¹⁹ The dependence of chemical reactions on the temperature is best described by the Arrhenius equation, which states that the higher the temperature, the faster a given chemical reaction will proceed.²⁰

Unlike existing laser systems for the treatment of acne that filter the heat by cooling means, some light-based systems do not use cooling means before, during, or after light emission. One system (Clear-Touch) allows direct deposition (by conduction) of heat from a nonoptical, exogenous source. It has been speculated that in addition to its role as a catalyst in the *P. acnes* inactivation, heat energy may open obstructive follicle pores. This factor may encourage the release of neutrophil, mononuclear cells, free fatty acids, hyaluronidase, and other proteases released by *P. acnes*, as well as *P. acnes* itself.²¹

Further support to the role of heat comes from Kjeldstad.²² Using near-ultraviolet light (330 to 410 nm), the author found that photoinactivation of *P. acnes* increased exponentially as the temperature increased in intervals of 10°C, 20°C, and 37°C. In contrast, decreased temperature during illumination increased the ability to form *P. acnes* colonies.

Treating skin disorder such as acne with laser/light-based devices is a multifactorial process that involves a complex photothermal reaction on the cellular-tissue level of the dermis-epidermis matrix. In cases of treating acne in areas such as the face, back, chest, or neck, laser/light parameters, such as pulse width, energy density, wavelength, and spot size, should be critically designed (manufacturer) and selected (physician) because the face and neck areas have zero tolerance for adverse side effects. Reported adverse side effects with current systems for the treatment of acne have been limited to temporary localized skin pigmentation, edema, and erythema.

Wavelengths' Role in the Treatment of Acne

Although sun exposure has a beneficial effect on acne symptoms, it was not clear until recently which wavelengths contribute to this favorable effect: UV, visible light, or the combination of both. UVA and UVB treatment was found to have a marginal beneficial effect, but it is potentially carcinogenic.²³

One of the main limitations of light therapy for acne is the fact that the photons have to penetrate through the epidermis before it can reach the depth necessary for activation of the porphyrins. Theoretically, blue light has the most effective visible wavelength for photoactivation of endogenous porphyrin component of *P. acnes* because the 407- to 420-nm band has the strongest porphyrin photoexcitation coefficient

(Figure 3). However, blue light has poor depth of skin penetration. Red light, however, in addition to its deeper penetration, albeit low extinction coefficient, may have anti-inflammatory properties by influencing cytokinase release from macrophages.²⁴

Research has shown in vitro that the viability of *P. acnes* relates inversely to light intensity. According to an action spectrum for the inactivation of *P. acnes*, the sensitivity of *P. acnes* is highest for shorter wavelengths and decreases with increasing wavelength.²⁵ Interestingly, the effect of UV light on lymphocytes was found to be dose dependent: When using high density, UV light is lymphocytotoxic and can diminish inflammation; in contrast, using low-density UV can encourage inflammatory reactions.^{26,27} Whether the end result will be clearance or flare up of the acne lesions depends on the nature of the lesions and the balance between the contributions of each UV densities in the photobiology process. It also depends on the organism, which may not always be *P. acnes*.²⁸

Recently, mixed blue (450-nm) and red light (660-nm) with blue light alone were compared. The authors concluded that phototherapy with mixed blue-red light, probably by combining antibacterial and anti-inflammatory action, is an effective means of treating acne of mild to moderate severity, with no significant short-term adverse effect.²⁹

In order to define the most effective wavelengths of visible light on acne, Sigurdsson et al.¹⁶ found that all "full-spectrum" green and violet light sources improved the acne, leading to 14% ($p > 0.10$), 22% ($p < 0.05$), and 30% ($p < 0.02$) acne lesion clearance, respectively. Although not statistically significant, there was a tendency in most scores for violet light to be the most effective between the three different light sources.

Clinical Experience Using Light Therapy in the Treatment of Acne

Clinical experience with lasers/light-based technology for the treatment of acne is in its infancy. Nevertheless, from scientific publications, testimonials, and clinical trials collected in the past decade, it becomes evident that light therapy—alone or with combination with other remedies—yields a significant decrease in acnes symptoms.

In one of the most recent study, Kawada et al.³⁰ studies 30 patients with mild to moderate acne. Patients were treated with a high-intensity, narrow-band, blue-light source twice a week for up to 5 weeks. The authors reported an reduction of 64% in acne lesions. Interestingly, in vitro investigation revealed that irradiation from this light source reduced the

number of *P. acnes*, but not *Staphylococcus epidermidis*, that were isolated from the acne patients.

In a multicenter study,³¹ a total of 35 patients with papulopustular acne were treated twice a week with the high-intensity metal halide lamp. Treatment dose was 90 mW/cm² of visible light. During each treatment, the patient's face or back was exposed to light for 10 minutes. At 2 months after the final treatment session, patients returned to the centers for clinical assessment. After eight biweekly treatments, 80% of the patients showed significant improvement of non-inflammatory, inflammatory, and total facial lesions. Inflammatory lesion count decreased by a mean of 60%. At 2 weeks after the last treatment, the count had even further decreased to almost 70%. No side effects of the treatment were observed. The authors reported that skin temperatures increase in a few cases by less than 1.5°C. In 20% of the patients, there was no treatment effect. The lack of response in these patients may be attributed to the existence of deep acne cysts or to the existence of non-*P. acnes* bacteria.

Meffert et al.³² used a high-energy broad-spectrum blue-light source that consist of both visible blue light and UVA with a wavelength of 410 to 420 nm. They reported marked improvement in patients with pustule acne after 10-dose treatments (cumulative dose 325 J/cm²).

In a recent article, Papageorgiou et al.²⁹ described phototherapy for acne comparing a mixed blue and red light (415 and 660 nm) with blue light alone. With daily treatment for 3 months (cumulative dose of 200 J/cm²), they achieved 58% reduction in inflammatory lesion count but only 25% with white light. The combined blue-red light was generally better than blue light alone. Side effects were minimal in all groups.

A different therapy approach is to target and destroy the sebaceous gland by a laser. With the exception of systemic Isotretinoin, traditional acne remedies do not alter the sebaceous gland from which acne lesions originated. Paithankar et al.³³ used a 1450-nm diode laser in conjunction with cryogen spray cooling to treat patients with acne on the upper back area. Four treatments were performed at 3- to 4-week intervals with lesion counts done at each visit. Additionally, biopsies were obtained in 4 of the 24 study participants. A statistically and clinically significant reduction in lesion counts was seen in the treated side when compared with the control side at the 6-, 12-, and 24-week follow-ups after the fourth treatment. Average lesion count was decreased from 5.43 to 0.43 on the treated sites. Side effects were transient and few.

Elman et al. (personal communication, September 2002) studied 19 patients with mild to moderate acne.

Using a new pulsed flash lamp acne clearance system, patients received eight biweekly treatments over a 4-week period, with two follow-up visits. No other remedies were given to the patient during the course of the treatment. All patients demonstrated a significant reduction (approximately 80%) in the number of acne lesions. The improvement persisted 3 months after the last treatment.

PDT for the treatment of acne was reported recently. In an open-label prospective study by Hongcharu et al.,³⁴ acne was treated with topical δ -aminolaevulinic acid-PDT and red light (550 to 700 nm). There was evidence of clearance that lasted for 20 weeks after multiple treatments and 10 weeks after a single treatment. Additionally, the *P. acnes* appeared to be significantly decreased for at least 20 weeks after treatment. Some side effects of the treatment included pain during treatment, a transient inflammatory reaction, and hyperpigmentation that completely faded over several weeks. Thus, PDT may be effective treatment but is associated with adverse side effects.

Clinical Guidelines and Considerations

In selected patients with inflammatory acne, light therapy can be the treatment of choice. During the first visit, the physician should assess the affected area. The criteria for therapy will include acne type and severity. Burton scale for grading acne severity is shown in Table 3.

Before initiating the treatment, the patient or patient's guardian should sign an informed consent. In addition, the physician should speak with the patient about realistic expectations and treatment limitations. Pretreatment preparations should include rinsing and cleaning of the treatment area with soap and water and drying the skin surface with a soft cloth. Photographs should be taken at baseline, at every two treatments, and at the follow-up visits.

Treatment protocol usually includes 8 to 10 biweekly treatments and two follow-up visits: 1 and 3 months after the last treatment. In some cases, more treatments may be needed. A single treatment usually lasts 20 to 25 minutes. Whereas some light sources

(i.e., ClearLight, DermaLux) require no physical contact with the affected area during treatment, other laser/light sources (i.e., ClearTouch, Smoothbeam, PhotoGenica) require the applicator handpiece full contact with the skin during the treatment. In most cases, treatment is done while the patient is lying down on a comfortable bed (Figure 4). During the treatment, the patient's eyes should be protected with dark glasses.

Common affected acne areas are the face, neck, chest, and back. In situations in which acne is on the back and rubbing topical cream is difficult, light therapy might be the therapy of choice. From preliminary results done on the back area with a laser system, fewer treatments might be needed.³³

From clinical experience with light-based systems gained in Israel and the United States, a maintenance treatment may be necessary in some patients 6 months after the last treatment. Manufacturers of the systems cite a clearance of greater than 50% in 85% of the patients, with 20% of the patients possibly showing approximately 90% quantitative clearance (eradication) of the inflammatory acne lesions. The nonresponders rate is expected to be approximately 10% to 20%.

Most clinicians have reported improvement (a reduction in size and the number of inflammatory lesions and less oily skin) after the 2nd week of treatment. In many cases, improvement is more



Figure 4. Light-based acne therapy (courtesy of Monica Elman, MD).

Table 3. Burton Scale

Grade 0		Total absence of lesions
Grade 1	Subclinical acne	Few comedones only visible by close examination
Grade 2	Comedonal acne	Comedones and mild inflammation
Grade 3	Mild acne	Inflamed papules and erythema
Grade 4	Moderate acne	Many inflamed papules and pustules
Grade 5	Severe nodular acne	Deep nodules with inflamed papules and pustules
Grade 6	Severe cystic acne	Many nodule cystic lesions with scarring



Figure 5. Before and after results of light therapy (courtesy of Monica Elman, MD).

evident 2 to 3 weeks after the eighth treatment. It has been speculated that destruction and elimination of *P. acnes* continues for a few weeks after the last treatment, and the self period of time required for the rebuilt of the initial concentration of the bacteria is the period of time that the effect is going to last. Figure 5 depicts before and after results of a patient who underwent light therapy.

Although the amelioration of acne by light therapy is comparable to the effects of traditional antibiotics, acne clearance occurs at a significantly faster rate (4 vs. 8 to 12 weeks) and without adverse side effects. Figure 6 demonstrates the acne inflammatory lesion clearance rate and a comparison for conventional topical and oral antibiotic treatments.

The latest arm therapy that is being studied in several centers around the world is the effectiveness of combined light–drug therapy. Topical therapy such as benzoyl peroxide, topical retinoids (not applied before light treatment), or chemical peel (salicylic acid 30% or glycolic acid, 20% to 35%) applied between light treatments is reported to have a beneficial effect. In cases of patients with multiple lesions such as comedones, papules, and postules, combined light therapy with exfoliative or keratolytic agents may be beneficial. Light therapy may be helpful as a first line of treatment in cases in which the physician would like to reduce the dose of oral Isotretinoin. This precursory therapy may reduce the flair up that is normally linked to Isotretinoin regimen.

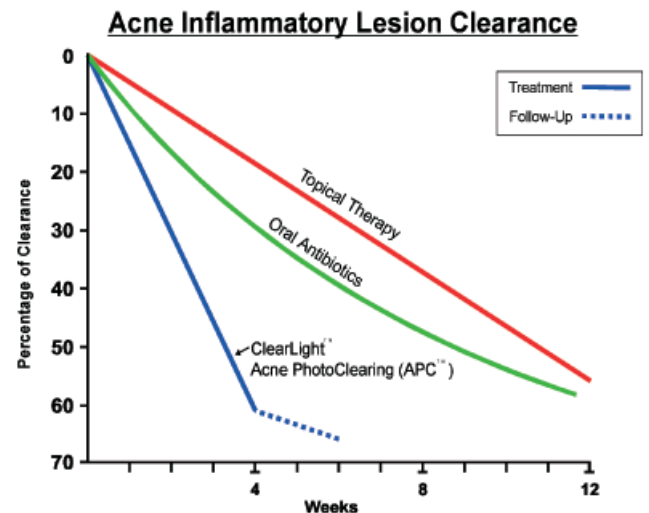


Figure 6. Multicenter clinical results: inflammatory acne lesion counts for light-based treatments and comparison for conventional topical and oral antibiotic treatments.

Conclusion

Acne vulgaris is a common skin disorder that poses significant medical, social, and psychological problems to the patient. Although for many years the favorable effect of sunlight on acne symptoms attracted the intention of the medical scientific community, the use of light therapy for the treatment of acne was uncommon and technologically neglected.

Although topical and oral therapies are considered the first line of treatment, significant adverse side effects or bacterial resistance may exist. Thus, there is an unmet need for well-tolerated therapy that provides effective acne clearance without the risk of side effects.

Recently, a significant advancement in photobiology and laser/light-based technology created new possibilities to treat acne. Based on successful in vitro and in vivo studies and human clinical trials conducted in the last 5 years, it is evident that the amelioration of acne with light-based therapy is comparable to the effects of oral antibiotics, and improvement is maintained for several months. Furthermore, it appears that these systems offer faster resolution and fewer side effects and lead to patient satisfaction.

Laser/light-based therapy for the treatment of acne is a fast-growing therapeutic modality. In order to establish its recognition, more clinical studies are needed to elucidate its efficacy and safety in different acne symptoms in a larger set of patients and in longer follow-up periods. These studies should compare conventional therapy with light therapy or to combine therapy (light + drug) modalities. The results of such studies will enable the clinician to choose/offer the most effective therapeutic coverage for the treatment of acne.

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