







REVIEW ARTICLE

Treatment of mild to severe acne with 1726 nm laser: A safe alternative to traditional acne therapies

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Abstract

Introduction: Acne is the most common reason for dermatology consultation in adolescents and young adults. Consultation is often delayed despite unsuccessful self-treatment. Postponing effective treatment places acne sufferers at higher risk for permanent acne scars and post-inflammatory pigment changes.

Aim: This review discusses clinical challenges with present therapeutic options for acne treatment and the role of a 1726 nm laser for acne.

Methods: Current acne treatment guidelines were reviewed. A literature review was conducted for trials of light-based acne therapy. The selectivity of previous light-based therapies was reviewed.

Results: Available acne therapy is effective, but treatment-related side effects are common. Acne treatment guidelines do not include recommendations for light-based treatments. Different types of light-based treatments have been tried but until now no wavelength specifically targeted sebaceous glands.

Conclusion: The 1726 nm laser is safe and effective for treating mild to severe acne in all Fitzpatrick skin types. Acne resolution is apparent within the first month and improves for up to 2 years beyond treatment.

KEYWORDS

acne vulgaris, laser, photo thermolysis

1 | INTRODUCTION

Acne vulgaris ("acne") is a multifactorial skin disease characterized by a prolonged course of recurrent breakouts with significant social, psychological, and physical consequences.^{1,2} Acne is seen in all

age groups, with most prevalence in adolescents and young adults.¹ Worldwide, the incidence and prevalence of acne continue to increase.³ In our image-focused culture, peer status is linked to appearance, which creates anxiety and depression in adolescents and adults with acne.^{4,5} Adults with severe acne are more likely to be

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unemployed when compared to age-matched controls.⁶ Appearance bias may be more than just cultural; there is research to suggest evolutionary and subconscious influences.^{7,8}

Acne is the most common reason for dermatology consultation in adolescents and young adults,⁹ but even moderate to severe acne sufferers may not seek professional advice for a year or longer despite unsuccessful self-treatment.^{10,11} Lack of early effective treatment places acne sufferers at higher risk for permanent skin changes such as erythema, post-inflammatory hyperpigmentation (PIH), and atrophic or hypertrophic scar formation.^{10,11}

Current treatment guidelines^{12,13} rely on topical and systemic therapies that are neither effective nor well tolerated in all patients. Interest in the potential of light-based therapies as alternative treatments is growing. This review discusses clinical challenges with present therapeutic options for acne treatment and the role of a 1726 nm laser device for acne.

2 | METHODS

Seven physicians plus an advisor with international scientific experience (the authors) met to discuss the literature on acne treatments. All physicians are dermatologists who were chosen for their clinical experience and medical expertise in treating acne-affected people of all ages. Following a discussion of the limitations of medical therapy and literature reviews of light-based therapy, the panel discussed the best practice use of a newly FDA-approved 1726 nm laser for acne treatment. The panel's expert opinions regarding the use of the 1726 nm laser to optimize acne outcomes were summarized.

2.1 | Literature review

A literature search of the National Library of Medicine PubMed Database for studies published from 2010 to February 2023 was conducted. Randomized controlled trials of novel acne treatments using light-based and laser therapy to prevent disease progression were reviewed. Inclusion criteria were English language studies, consensus papers, and other reviews that focused on light-based therapy designed to diminish the impact of the pilosebaceous inflammation that leads to acne. Exclusion criteria were articles with no original data (unless a review was deemed relevant) or published in a language other than English. Also excluded were studies that combined medical treatment with light-based modalities (such as isotretinoin, platelet-rich plasma, growth factors, facial peels, and others), or studies designed to measure improvement in acne scars.

3 | RESULTS

3.1 | Medical treatment for acne

A current understanding of the pathophysiology of acne helps to grasp the rationale for therapy. Acne comedones, papules, pustules,

and nodules are primarily the result of four factors: hyperkeratinization of the pilosebaceous duct resulting in duct obstruction; ductal colonization with *Cutibacterium acnes* (*C.acnes*); androgen-driven increases in sebum production; and pilosebaceous unit inflammation.^{2,12-15} Standard topical and systemic therapies target one or more of these features.

The decision to treat with one medication or multiple medications depends on acne severity, though there is no standardized acne-grading method.¹³ Comedonal acne is noninflammatory. Inflammatory acne, which can be mild, moderate, or severe, refers to papules, pustules, nodules, and cysts. Acne severity can be rated clinically on a scale of 0–4, with 0 indicating “clear”; 1 is comedonal acne; 2 is mild–moderate papulopustular acne; 3 is severe papulopustular acne or moderate nodular acne; and 4 is severe nodulocystic acne or conglobate acne.¹³

3.1.1 | Topical therapy

Improvement in Type 1 and Type 2 acne can be achieved with topical treatment. A single topical agent, such as benzoyl peroxide (BPO) or a low-strength retinoid,¹² may be sufficient. The bactericidal activity of BPO is especially effective in controlling *C.acnes*, which plays a pivotal role in acne. *C.acnes* increases the proliferation and differentiation of keratinocytes; it activates innate immunity via toll-like and protease-activated receptors, which trigger the production of pro-inflammatory cytokines.¹⁶

Retinoids work by normalizing keratinization and reducing inflammation. Type 2, or mild papulopustular acne, may require a combination of two topical agents such as BPO plus a retinoid, or fixed combinations of a topical antibiotic + BPO, or a topical antibiotic + a retinoid.^{12,13} Once control has been achieved, topical retinoids are ideal as monotherapy for long-term maintenance in all types of acne as they have the unique ability to prevent the formation of microcomedones.¹⁷

3.1.2 | Systemic therapy

Antibiotics are the most frequently added systemic therapy for acne that has not responded well to topical remedies. More antibiotics are prescribed by dermatologists than any other specialty.¹⁸ For moderate to severe acne, tetracycline-derived antibiotics—minocycline and doxycycline—are most often used in combination with topical agents. Although their use is intended to reduce *C.acnes* numbers, oral tetracycline derivatives have anti-inflammatory qualities that add to their efficacy.¹⁹ Due to increasing levels of bacterial resistance, oral antibiotics should be used for short periods of time, 3–4 months or less.^{12,13,16}

Hormonal therapies are effective acne treatment adjuncts for women, yet oral antibiotics are prescribed more frequently.²⁰ Hormonal therapy can be achieved with spironolactone or oral contraceptives, which downregulate the effects of androgens on sebum production. Spironolactone, originally developed as a

diuretic, has antagonistic effects on androgen and progesterone receptors. Spironolactone is helpful for adult-onset acne in women and in women with acne due to polycystic ovary disease. It can be safely used long-term in healthy women.^{21,22} Oral contraceptives that contain estrogen and progestin reduce free testosterone which diminishes sebum production. In the United States, a few specific estrogen/progesterone combination oral contraceptives²¹⁻²³ have been approved for acne treatment. Improvement with these agents may take several months. Progestin-only oral contraceptives, and progestin-containing long-acting implants or depot products, can make acne worse.²³

Isotretinoin

Isotretinoin should be considered when a patient with moderate to severe acne fails combination topical therapy plus a systemic agent. It can be started as first-line therapy in a severely affected patient.^{12,13,24} Isotretinoin normalizes follicle keratinization, inhibits *C. acnes*, reduces inflammation, and reduces sebum secretion by shrinking sebaceous glands. It is the only disease-modifying acne therapy. When dosing and length of treatment are sufficient, there is the likelihood of durable shrinkage of the pilosebaceous unit that persists once the drug is discontinued,²⁵ resulting in prolonged and often permanent acne resolution. Isotretinoin does not permanently remove all sebaceous gland functions. Sebaceous gland function will renormalize to levels enough to sustain sebum production but not enough for excessive bacterial proliferation.

4 | LIMITATIONS OF CURRENT ACNE TREATMENTS

Available acne medications are effective, but adverse effects and delayed onset of action limit their use. The demographic with the most acne, adolescents and young adults, may become impatient with their perceived slow progress. Topical products such as BPO and low-strength retinoids routinely cause dry, flaking skin, that, although temporary, prompts many patients to discontinue therapy before optimal effects are achieved. In a study of 250 patients with a mean age of 18.6,²⁶ 45% abandoned therapy before an adequate therapeutic trial. Lack of response was cited by 62%, and 38% reported unacceptable side effects. Patients with severe acne were more likely to quit topical treatment early due to a lack of response.²⁶

Beyond their skin irritant effects, topical retinoids may pose additional risks in adolescent and young adult women—groups with high pregnancy rates. Adapalene and tretinoin are both pregnancy category C, meaning animal data suggest fetal risks though human pregnancy data are lacking. Tazarotene is pregnancy category X, indicating it should not be used during pregnancy. The newest topical retinoid, trifarotene, has not been assigned a pregnancy-risk category.

Pregnancy or plans to become pregnant also limit use of tetracycline-derived antibiotics. Minocycline can cause skin and mucosal pigment changes, and it has been associated with a lupus-like syndrome with a higher incidence in young women.²⁷ Common side

effects of tetracycline-derived antibiotics are photosensitivity, gastrointestinal upset, dizziness, and headaches. Pseudotumor cerebri (PTC) is a risk with this class of antibiotics and it can occur in children.^{28,29} Subtle symptoms and early fundoscopic signs of increased intracranial pressure can be missed, allowing unrecognized PTC to progress to visual impairment.^{28,29}

Systemic strategies with hormonal therapy have considerable side effect potential. Spironolactone leads to dose-dependent menstrual irregularities in 15%–30% of patients.²¹ In lab animals, spironolactone has been shown to feminize a male fetus.²¹ Oral contraceptives are often associated with nausea, breast tenderness, and breakthrough bleeding. Even the small chance of a thromboembolic event may discourage oral contraceptive use.

Despite decades of use, controversies still exist regarding the use of isotretinoin. As with oral tetracyclines, isotretinoin poses an increased risk of PTC²⁹ and the two should not be used together. Almost all patients treated with isotretinoin develop mucocutaneous and eye dryness that can be severe. Myalgias, liver enzyme abnormalities, and elevated triglycerides have been reported.^{24,25} Severe depression has been reported though there is controversy about whether this is drug-related or due to the severe acne for which isotretinoin is prescribed.³⁰ Retinoid embryopathy is a known side effect and the use of isotretinoin involves the added administrative burden of enrollment in the iPledge program,³¹ an FDA-mandated safety program intended to diminish the risk of isotretinoin's teratogenicity. Based on histological data that demonstrate a drastic decrease in the size, shape, and lipid content of sebaceous glands while undergoing isotretinoin treatment,^{32,33} patients who can tolerate a long course of isotretinoin are rewarded with dramatic disease improvement.

5 | ENERGY DEVICES FOR ACNE

Energy-based devices fill a therapeutic need for patients who cannot tolerate or who do not respond to conventional acne therapy. Acne treatment guidelines^{12,13} do not include recommendations for energy-based devices. Published summaries of light-based trials^{21,34-39} underscore increasing interest in energy modalities.

A 2016 Cochrane review of randomized controlled trials of light treatments for acne concluded reliable synthesis of data could not be determined due to differences in patient selection, different wavelengths used, varying total doses and a number of sessions, and lack of standardized outcome measures.⁴⁰ More than half of the studies in the Cochran review were industry sponsored. Of the energy device trials reviewed, photodynamic therapy (PDT) was the most widely studied and was thought to have some usefulness.⁴⁰ In an evidence-based review of photodynamic therapy,³⁸ moderate to severe inflammatory and non-inflammatory acne responded to red light as a light source when the skin was pretreated with a photosensitizer for several hours before light exposure. PDT appears to be effective, but it can be painful, and the durability of response over time is unclear. Light-based therapies, their mechanisms of action, and common side effects are listed in Table 1.

TABLE 1 Summary of light-based procedures that have been used for inflammatory acne.

Device	Mechanism of action	Side effects
Fractional CO ₂ laser	Photothermolysis of sebaceous glands	Pain; erythema; bleeding; transient PIH
Potassium titanyl phosphate (KTP) laser	Thermal injury to sebaceous glands; reduction of <i>C. acnes</i>	None reported
Pulsed dye laser (PDL)	Targets dermal blood vessels; increases growth factor	Pain; erythema; edema; peeling; crusting; blistering; transient PIH
1064nm Nd:YAG Infrared laser	Destroys sebaceous glands; reduces perifollicular stratum corneum; reduces inflammation	Erythema; dryness; burning; crusting; transient PIH
1450nm Nd:YAG Infrared laser	Destroys sebaceous glands	Erythema; edema; transient PIH
1540nm infrared laser	Destroys sebaceous glands	Erythema; edema; heat sensation
1565nm nonablative fractional laser	Destroys sebocytes; reduces <i>C. acnes</i>	Erythema; edema, crusting; transient PIH
800nm diode laser with gold microparticles	Selective destruction of pilosebaceous infundibulum and glands with gold-coated silica microparticles with strong absorption at 800nm	Erythema; overall well-tolerated
Blue light 407–420nm	Photoactivation of bacterial porphyrins; reduces <i>C. acnes</i> ; reduces inflammation	Erythema; stinging
Red light 620–700nm	Anti-inflammatory effects	Few side effects by itself; mild to severe discomfort following use of a topical sensitizer
Intense pulsed light (IPL) 400–1200nm	Photothermolysis of sebaceous glands; activation of bacterial porphyrin; reduces <i>C. acnes</i>	Transient PIH; can worsen nodulocystic lesions
Photopneumatic therapy (IPL with suction)	Expels comedones with suction; thermal destruction of follicles; reduces <i>C. acnes</i>	Erythema; edema
Photodynamic therapy (PDT) after application of topical aminolevulinic acid (ALA) or methylaminolevulinate (MAL)	Destroys sebaceous glands; reduces <i>C. acnes</i> ; reduces inflammation	Pain (intolerable with ALA 20%); erythema; edema

5.1 | Novel 1726 nm laser for acne

Table 1 illustrates that reduction of sebum production is the primary mechanism of action in light-based therapies. Energy delivered by lasers increase the skin's temperature because water is abundant in skin, and water's absorption coefficient is significant with infrared lasers.⁴¹ Sebaceous glands are injured by the increased temperature, but discomfort and collateral damage to other skin structures cannot be avoided.⁴¹

A better approach is to selectively deliver energy to specific chromophores within the sebaceous gland that has a higher absorption coefficient than water. Sebum in the sebaceous gland is a favorable target because it has a narrow absorption peak, higher than water, at 1726 nm.^{41,42} In 2012 Sakamoto et al. demonstrated optical pulses with wavelengths between 1700 and 1720 could destroy sebaceous glands in ex vivo human facial skin, with minimal damage to surrounding tissues.⁴²

A novel infrared diode laser device with a nominal wavelength of 1726 nm was designed to generate a significant and rapid temperature rise inside the sebaceous glands to heat sebum, producing a controlled thermal injury of the glands.⁴¹ As heat causes pain, the addition of skin cooling minimizes skin discomfort. Thermal protection for the epidermis and superficial dermis is provided by a temperature-controlled skin-contact cooling window.⁴¹ In an in vivo

model, human facial skin from around the ear was exposed to the energy settings determined to be ideal. The treated area was excised 5 days later. Total necrosis of the sebaceous gland was seen, with sparing of the epidermis and of the follicular epithelium.⁴¹

Performance testing to assess the safety and efficacy of the new 1726 nm laser was done in an open-label, prospective, multicenter clinical study prior to FDA approval.⁴³ A total of 104 patients, 57% female, 43% male, aged 16–40, with mild (*n*=1), moderate (*n*=81), or severe (*n*=22) acne were enrolled. More than 20% of those enrolled had severe acne and 28% of total patients were males aged 16–19. The study's primary objective was to show that ≥50% of subjects attained treatment success defined as a reduction ≥50% in inflammatory acne lesions 12 weeks after their final treatment compared to baseline. Treatment consisted of a total of three 30-min laser facial treatments spaced 2–5 weeks apart. Photographs taken throughout the study were sent to a panel of three trained expert physicians for Investigator Global Assessment (IGA) grading. Noninflammatory and inflammatory acne lesion counts (ILC) were performed by lesion counters who were blinded to the study design. Results obtained at 12 weeks after the last treatment are summarized in **Table 2**.

Subjects were also assigned to subgroups by age, gender, Fitzpatrick skin type, and baseline IGA. Responder rates and device-related adverse events within these three subgroups were

TABLE 2 Efficacy of a novel 1726 nm laser 3 months after a total of three treatments.

Efficacy measure	Percent of subjects improved 12 weeks after third treatment
IGA improvement 1+	87%
IGA improvement 2+	47%
IGA improvement clear/almost clear	36%
Inflammatory lesion count (ILC)	91%
ILC improvement >50%	80%
Nodule count reduction	67%
Comedonal count reduction	32%

compared. Adverse events were mild, and the rates were similar in all subgroups. Erythema (100% of subjects) and edema (98% of subjects) were transient, resolving within several hours to several days. Acne purging was the third most common adverse event reported by 45.2% of patients. All purging events were mild except for one described as moderate in a participant with a severe IGA at baseline. Mild dryness was experienced by 18.3%. There was no blistering, hyperpigmentation or hypopigmentation, or scarring. No patient with Fitzpatrick type V or VI skin dropped out of the study. Topical pre-procedural numbing was not performed. There were no differences in discomfort levels by skin type, with median discomfort levels rated as 5.0–5.1 (0–10 scale).⁴³ The results of this report that led to FDA approval are similar to those published by Goldberg et al in 2022.⁴⁴ In a study of 17 patients, statistically significant reductions in inflammatory lesions were seen beginning 4 weeks after treatment. Improvement continued well beyond the initial study. Subjects who continued follow-up showed progressive improvement, with a 97% reduction in inflammatory lesion counts at 2 years.⁴⁴

6 | DISCUSSION

Nonadherence with topical and systemic therapy is high due to complicated, multistep treatments, topical and systemic side effects, and administrative burdens. Undertreatment of acne leads to pigment changes and scarring. Permanent acne scarring occurs across all levels of acne severity, a critical finding for practitioners who treat acne.¹¹ Of those affected by acne scarring, 20% fear that scarring will affect their employability.¹¹

Until now, the benefits of laser therapy for acne came at the cost of undesirable skin discomfort and skin damage due to a lack of selectivity for sebaceous glands. Selective photothermolysis using a new 1726 nm laser ensures effectiveness and safety in mild to severe acne while managing discomfort with a contact cooling system. The 1726 nm laser was studied and is approved for ages 16 and above. Unlike the dozens of laser trials using non-selective wavelengths, pigment changes were not observed with the 1726 nm laser. Melanin is not a clinically meaningful absorbing chromophore at 1726 nm, so the new laser is safe for all skin types.

Adequate, early treatment is the key to acne remission without physical, social, or emotional sequelae. There are many effective topical products to treat acne and three options for systemic treatment. Of all available medications, only isotretinoin is disease-modifying. The 1726 nm laser may have a similar long-term effect on sebaceous glands as does isotretinoin. Both treatments have histological data that show a marked decrease in the size, shape, and lipid content of sebaceous glands in human skin after treatment.⁴⁴ However long-term follow-up of patients treated with 1726 nm laser compared to those treated with oral isotretinoin may provide conclusive evidence.

The new 1726 nm laser may represent a paradigm change in acne treatment, providing safe, effective, and convenient treatment for mild to severe acne in all skin types.

6.1 | Limitations

The review discusses clinical challenges with present therapeutic options for acne treatment and the role of a 1726 nm laser for acne. The review was limited to exploring the role of a 1726 nm laser for acne in view of currently used treatments. A review comparing various laser treatments is outside the scope of this paper.

Evidence-based guidelines rate the quality of evidence to support treatment options. Clinical consensus recommendations utilize expert opinion based on the experience of what treatment works well in particular situations. Laser treatment studies are challenging to design due to the difficulty in assessing a control group; patients often serve as their own controls. The 1726 nm laser was recently approved in 2022 which has limited widespread real-world clinical experience.

6.2 | Future directions

A clinical trial (clinicaltrials.gov identifier: NCT05430464) is recruiting participants to assess the benefits of the 1726 nm laser versus sham laser treatment.

AUTHOR CONTRIBUTIONS

DJG and AA performed the research for this manuscript. DJG, AA, ACB, MHG, ABL, MSL, JHM, and AR contributed to the development of the manuscript, reviewed it, and agreed with its content.

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DATA AVAILABILITY STATEMENT

The data supporting this manuscript's findings are available in PubMed [<https://pubmed.ncbi.nlm.nih.gov/>] and Google Scholar [scholar.google.com].

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