Journal of Cosmetic and Laser Therapy, 2014; Early Online: 1–7

REVIEWS OF TREATMENT STUDIES

Acne vulgaris and light-based therapies

SOPHIE MOMEN[1] & FIRAS AL-NIAIMI[2]

[1]*Skin Clinics, and* [2]*Royal Free London NHS Trust, London, UK*

Abstract
Acne vulgaris is a common condition which remains challenging to treat in some cases. Laser and light-based therapies offer an alternative to medical therapies with the advantage of high compliance and relatively low side-effect profile. Light-based therapies in acne exert their effects through photochemical, photothermal, or a combination of both mechanisms. This article explains the mode of action for each light-based modality and examines the current evidence in this field.

Key Words: *lasers and light sources, PDT*

Introduction

Acne vulgaris is one of the most prevalent skin disorders, which often occurs in a large number of individuals during their adolescent years. It has the potential to cause significant scarring and psychological impact (1). There are a large number of treatment options available to patients at present; however, these are not without side-effects and in many cases the disease can be resistant to therapy, hence the desire for additional, alternative treatment options. Non-compliance, the lack of desire for systemic therapy, coupled with the desire for the use of modern technology has led to an increase in the demand for alternative non-medical therapies in acne. Of late, interest in lasers and other light-based treatments has increased. One of the main advantages of the use of lasers in acne is the high degree of compliance and the negligible rate of potential systemic adverse events.

The mechanisms of light-based therapies in acne could be divided into photochemical effects (with or without the use of exogenous photosensitizer), photothermal effects, and the combination of both. An alternative approach is to divide the effects of light-based therapies on specific targets in the skin, namely the *Propionibacterium acnes* (*P. acnes*), the follicular infundibulum, and the sebaceous glands. It is worth mentioning here that therapies directed at either of these targets will have a degree of anti-inflammatory effects, leading to an overall improvement in the treatment of acne.

Ultraviolet (UV) phototherapy is not often used in the treatment of acne due to the carcinogenic potential, and its mechanism of action is likely to be related to the production of superoxide anions, as well as membrane damage and single-strand breaks in DNA (2). Desquamative effects are also likely to play a role as well as a mild photochemical effect on the superficially located *P. acnes*. Both visible and UV light sources have been reported to result in a reduced number of lesion counts (3). Endogenous porphyrins within *P. acnes* are thought to absorb light at specific wavelengths which then produce phototoxic effects in the form of singlet oxygen production resulting in bacterial destruction (4). Current hypothesis regarding infrared lasers is that they are thought to momentarily damage sebaceous glands via thermal effects (5). This article explains the effectiveness of laser and light therapy in the treatment of acne. The article does not cover the treatment of acne scarring with laser and light devices.

Blue and red light

Low-level continuous lights in the form of continuous, non-coherent blue and/or red light-emitting diodes (LEDs) were known to be used in acne due to their photochemical effects. With pulsed systems, low fluences can exhibit similar photochemical effects depending on the tissue oxygen availability and may require an extrinsic photosensitizer or multiple passes in comparison to the continuous-output LEDs.

Correspondence: Dr. Firas Al-Niaimi, Consultant Dermatologist, Royal Free London NHS Trust, London, NW8 8AF, UK. E-mail: firas55@hotmail.com

(Received 19 June 2014; accepted 9 November 2014)

ISSN 1476-4172 print/ISSN 1476-4180 online © 2014 Informa UK, Ltd.
DOI: 10.3109/14764172.2014.988727

Although blue light has poor skin penetration (less than 100 micron), at a wavelength of 407–420 nm it exhibits the strongest porphyrin photoexcitation coefficient and thus is the most effective wavelength to photoactivate the endogenous porphyrins contained in *P. acnes* (6). The coproporphyrin, the main porphyrin produced by the *P. acnes*, acts here as a chromophore. An *in vitro* study demonstrated that blue light activation of porphyrin led to structural membrane damage in *P. acnes*, suggesting cell death. Culture growths were indeed decreased 24 h after one illumination with intense blue light at 407–420 nm. Growth was reduced by 4–5 orders of magnitude further with 2nd and 3rd illuminations of light (7).

One of the main limitations of blue light is its poor penetration and a degree of loss secondary to scattering or melanin absorption, and its main target is therefore likely to be in the follicular infundibulum.

Red light, however, penetrates the skin at a deeper level up to the sebaceous gland and is thought to have anti-inflammatory properties by influencing the release of cytokines from macrophages as well as photothermal effects directly aimed at the sebaceous glands (8). There have been a number of studies involving both blue and red light in the treatment of acne. Most were open-labeled with few split-face comparative studies. The sample sizes were relatively small (20–50 patients) and all studies noted an improvement in acne lesions.

One study looked at red light alone; when used in a split-faced randomized controlled trial, there was a significant improvement in both inflammatory and non-inflammatory lesions (9).

Five open-labeled studies used the combination of blue and red light in 170 patients and were followed-up for a period of 2–3 months. In four of these studies, inflammatory lesions showed greater improvement than non-inflammatory lesions·

In summary, blue and red light may act synergistically in the treatment of acne due to bactericidal effects (blue light) and anti-inflammatory effects (red light).

Pulse dye laser

The 585/595-nm pulsed dye laser (PDL) targets oxyhemaglobin and results in selective photothermolysis of the dilated vessels that form a part of the inflammatory process in inflammatory acne (4). Additional mechanisms possibly include a photochemical effect on the porphyrins produced by the *P. acnes.* Porphyrins are activated via the delivery of yellow light, which results in phototoxic effects(4,6).

Fourteen studies using PDL to treat acneiform lesions have been reported in the literature. There were significant methodological differences between the studies; six studies used PDL therapy alone and five studies used PDL therapy combined with topical agents (5-aminolevulinic acid, methylaminolevulinic acid, clindamycin, and benzyl peroxide).

In the studies that used PDL in combination with topical agents, four cases reported an improvement in inflammatory lesions ranging from 30 to 80%. In cases of PDL used alone, three cases reported a significant reduction (53–86%) in inflammatory lesions. PDL did not significantly reduce the number of non-inflammatory lesions in any of the cases. Three studies reported PDL to have no significant change in the number of lesions when used alone or in combination with topical agents.

One study by Seaton et al. suggested that PDL had no effect on *P. acnes* colonization or sebum production (measured using the application of absorptive tape) (10). They did, however, note upregulation of transforming growth factor beta (TGF-beta). Given that this is a potent inhibitor of inflammation, this finding suggests that this laser may act through anti-inflammatory effects. It has also shown to inhibit CD4+T-lymphocyte-mediated inflammation. TGF-beta may also induce keratinocyte growth arrest which could possibly interfere with comedone formation. Sami et al. compared PDL/intense pulsed light (IPL) and LEDs in the treatment of 45 patients with moderate-to-severe acne. They found that a clearance of 90% of inflammatory lesions was achieved quicker with the use of PDL than that with IPL, which was more effective than LED (11).

The exact mechanism of how PDL works appears to be multifactorial. The photothermal effect on the sebaceous glands is achieved partly by heating the dermal microvasculature secondary to the oxyhemoglobin absorption. It is hypothesized that the generated heat leads to the induction of heat shock proteins (HSPs), such as HSP70, which in turn could play a role in TGF-beta production.

In summary, PDL is likely to work due to both photochemical and photothermal effects; although the ideal exact parameters are not yet established and the studies have shown conflicting and inconsistent results. The debate on the true efficacy and role of PDL in acne continues with mixed opinions on its place in and efficacy in acne.

Potassium titanyl phosphate

Potassium titanyl phosphate (KTP) 532-nm laser emits green-light-pulsed laser, which penetrates deeper than blue light. It activates porphyrins, which target *P. acnes* as well as cause non-specific thermal injury to the sebaceous gland. It therefore exhibits a photochemical as well as mild photothermal effect. It has been shown to have short-term results on acne lesions with few side-effects. Four open-labeled studies have assessed the effectiveness of the KTP laser in the treatment of acne. In a split-face, prospective controlled trial of 26 patients with moderate acne, Baugh and Kucaba reported that KTP laser was a safe and effective method in treating acne lesions (12). Results lasted up to 4 weeks after treatment, with a 21% reduction on lesion count at 4 weeks versus a 35% reduction at 1 week. Bowes et al. carried out a prospective, split-face study of 11 patients and noted a 36% reduction of mild-to-moderate acne lesions in comparison to two percent in the control side. Yilmaz et al. also supported the use of this laser in the treatment of mild-to-moderate acne in 38 patients. Their findings showed that there was no difference between once or twice weekly applications (13). Despite these studies, the results are generally for short term and this laser is not often used in the management of acne.

Infrared lasers

1450-nm and 1540-nm lasers

Infrared lasers penetrate deep into the dermis targeting water as their main chromophore. Water is the dominant chromosphere in the sebaceous gland, thus infrared lasers are thought to arrest the production of sebum and eliminate acne. Both the 1450-nm and 1540-nm lasers have been used in this manner (14). Seventeen studies reported the use of these lasers, twelve were open-labeled and five were randomized trials.

1540-nm laser

The 1540-nm Erbium glass laser is a mid-infrared laser and has effectively been used for treating acne lesions in four studies. A 78% reduction in acne lesions was observed in 25 patients after four treatments at 4-week intervals (15). Kassir et al. noted a similar reduction (82%) at 3 months in 20 patients who received treatments twice a week for 4 weeks (16). Angel et al. demonstrated the longest clearance effects of the 1540-nm laser (2-year follow-up) (17). The mean percentage reduction of 18 patients treated with four treatments at 4-week intervals was 71%, 79%, and 73% at 6-, 9-, and 24-month follow-up, respectively. Inflammatory acne was shown to improve by 68% in 15 patients with moderate-to-severe acne treated four times at 2-week intervals; however, there was no reported change in sebum production (18). Virtually no side-effects were reported with the use of this laser. It is likely that this laser exhibits its effects through non-selective heating of the sebaceous glands.

1450-nm laser

The 1450-nm laser was first used in a study of 19 patients with inflammatory acne in which traditional therapies had failed. A fluence of 14 J/cm^2 was used in three treatments at 4–6-week intervals and a 37% and 83% reduction in lesion count was observed after the first and third treatments, respectively. Side-effects included transient erythema and edema (19). A randomized split-face trial was carried out to compare two treatment fluences by Jih et al. Twenty patients received three treatments at 3–4-week intervals; after one treatment, the percentage reduction in mean acne lesion count was 43% (14 J/cm^2) and 34% (16 J/cm^2), and after the patients were followed up for 12 months the reduction in lesion count was 76% (14 J/cm^2) and 70% (16 J/cm^2) (20). Acne scarring and sebum production also improved.

The 1450-nm diode laser heats the upper mid-dermis to a depth of 500 micrometers and can result in thermal coagulation of the sebaceous lobule and the follicular infundibulum (4). It is thought to improve acne lesions via heating the sebaceous gland and reducing its activity. Perez-Maldonado et al. displayed an 18% reduction in sebum production (measured by Sebutape scores) in eight patients treated with the 1450-nm diode laser for three treatments over a period of 6 weeks (21). Contrasting results were seen in fourteen healthy subjects (without active acne), with this laser showing no significant reduction in sebum production (22).

A split-face bilateral paired study treated 11 patients with the 1450-nm diode laser at a fluence of 11 J/cm^2. One half was treated with a single pass consisting of stacked double pulses and was compared with a double-pass treatment of single pulses. The stacking of pulses was more effective in reduction of acne lesion count compared with the multi-pass technique (23). Lower fluences elicit less pain, while still effectively treating inflammatory lesions. Single-pulse multiple-pass methods might have a reduced chance of cryogen-induced transient hyperpigmentation in comparison to the standard high-fluence techniques.

Yeung et al. supported that multiple pass/lower fluence can still retain efficacy, but reduce post-inflammatory hyperpigmentation (24). Bernstein et al. performed a randomized split-face trial of six patients with papular acne, comparing single-pass high-energy treatment (13–14 J/cm^2) with double-pass low-energy treatments (8–11 J/cm^2) for four treatments at monthly intervals. Single-pass high-energy treatment exhibited greater reduction in lesion count (78% vs 67%); however, pain score was greater in the single-pass group (5.6 vs 1.3) (25).

The 1450-nm diode laser in combination with the 585-nm laser has been shown to be effective in the treatment of inflammatory acne, acne scarring, and post-inflammatory erythema in 15 patients. The addition of microdermabrasion to the 1450-nm diode laser showed no significant benefit for treatment effectiveness or pain in a randomized split-face trial of 20 patients (26).

Despite the results of the aforementioned studies, this laser is associated with a relatively high degree of pain and discomfort and is no longer considered a laser of choice in the treatment of acne by many laser dermatologists worldwide.

Photodynamic therapy

Photodynamic therapy (PDT) involves the use of a photosensitizer, which is taken up by the pilosebaceous unit and undergoes metabolism through the heme synthesis pathway resulting in the production of protoporphyrin IX (27). The activation of this pathway leads to the production of free radicals and singlet oxygen which are cytotoxic and accumulation of these in the epithelium and pilosebaceous unit lead to elimination of the *P. acnes* and modulation of the sebaceous gland and infundibulum. *P. acnes* cultures grown in the presence of aminolevulinic acid (ALA) led to a fivefold decrease in culture viability after 3 illuminations of high-intensity blue light. For PDT to be effective, light, oxygen, and a photosensitizer are required: 5-ALA or methylaminolevilunate (MAL), indocyanine green (ICG), and indole-3-acetic acid are used as photosensitizers. A light source can be LEDs, fluorescent lamps, lasers, sunlight, xenon flash lamps, arc lamps, and filtered incandescent lamps. *P. acnes* photoinactivation can be altered depending on the concentration of porphyrins, which is governed by the type of acne lesion, effective fluence, wavelength of the photons emitted, and temperature (28).

Twenty studies using PDT in acne were published (11 randomized and nine open-labeled trials). IPL source was used in four studies (one randomized split-face, open-labeled; one randomized open-labeled study, and one split-face pilot study). ALA was used in four cases and MAL in one case. Yeung et al. noted a 65% reduction in inflammatory lesions after 12 weeks following PDT in comparison to 23% reduction when using IPL alone (29). Similar findings were found by Rojanmatin et al. at 12-week follow-up in a split-face trial (30). The PDT side had 87% reduction in lesions in comparison to 66% reduction with IPL alone. Another split-face trial using ALA with IPL was studied by Santos et al. in 13 patients with 10 out of 13 patients using the combination treatment showing marked improvement in comparison to the IPL alone group. Different modalities were compared by Taub et al. They compared IPL, IPL and bipolar radiofrequency (RF), and blue light for activating ALA-induced protoporphyrin IX. ALA–PDT activation with IPL provided the greatest and longest lasting effects in comparison to RF-IPL and blue light (31).

Five studies used long-pulse PDL (one randomized controlled split-face single-blinded trial, one cross-sectional comparative controlled prospective study, one split-face open-labeled study, and one prospective randomized study). MAL was used in conjunction with long-pulse PDL in two studies and a significant reduction in lesion count in the PDT-treated areas was seen by Garcia et al. and Haersdale et al. A reduction in both inflammatory and non-inflammatory lesions was noted; however, erythema and edema were reported as significant side-effects.

An interesting study by Hongcharu et al. with ALA followed by irradiation with red light showed histological evidence of sebaceous gland hypotrophy with glandular destruction. Furthermore, ALA–PDT decreased *P. acnes* fluorescence, a marker for bacterial colonization, as well as sebum secretion post therapy. Despite such encouraging findings, some studies using ALA followed by red light have failed to show any significant reduction in sebum production or *P. acnes* colonization (32).

Red light was used in seven studies: two randomized controlled, investigator-blinded trials, and controlled trials and one randomized controlled trial. Two studies used ALA plus red light, which saw a significant reduction in lesions.

Of 18 patients studied by *Taub* et al. 11 were noted to have a 50% improvement and five to have a 75% improvement (31). Side-effects included erythema and peeling. Goldman et al. followed up 22 patients for 2 weeks and noted an improvement in lesion count with no reported side-effects. There was a greater response in the ALA–blue light group compared with that in the blue light group alone (33). The same author used short-contact ALA for 1 h with either an IPL source or blue light with relative clearance of the inflammatory lesions. Gold et al. also used short-contact ALA of 30–60 min in combination with blue light in moderate-to-severe inflammatory acne and noted a response rate of 60%.

Blue light was also used in combination with ALA in two studies. Itoh et al. used halogen light with a filtered band of 600–700 nm in combination with ALA in 13 patients with all patients showing an improvement in their inflammatory component (34).

MAL is a lipophilic derivative of ALA and may therefore have better penetration. Its use as a photosensitizer in acne therapy was used in two European studies: the first by Wiegell and Wulf; the second study by Horfelt et al. Both studies showed a modest improvement in acne lesions with occlusion time of 3 h.

Intense pulsed light

An IPL device delivers an intense source of light, the wavelength of which can be modified via the use of filters. The generated pulsed light is polychromatic and non-coherent, and the emitted light can be tailored to the treatment by alteration of the filtered light, pulse duration, and fluence. IPL technology works in single- and burst-pulse modes. In the single-pulse mode, the fluence will be delivered in single shot, whereas in burst-pulse mode fluence is divided into series of pulses with a delay between the pulses. The theory of treating acne lesions with IPL is based on the photochemical and photothermal (higher settings) effects on the bacteria-derived porphyrins, as well as the inflammatory cells that mediate an inflammatory cascade, heating of the sebaceous glands, and small vessels associated with the process (35). The photochemical effects are likely to occur due to the blue and red range of light emitted by the IPL, whereas the infrared range of light has more of a photothermal effect on the sebaceous glands and dermal vasculature. IPL was used in nine studies with mixed results. Elman et al. used 430–1100-nm source in patients with moderate acne and saw a 74% and 79% reduction in inflammatory and non-inflammatory lesions, respectively, following twice weekly therapy for 4 weeks (14). Lee et al. carried out a split-face control trial in patients with mild-to-moderate acne and noted a significant reduction in both inflammatory and non-inflammatory lesions in comparison to no treatment (36). A further split-face trial with the use of benzoyl peroxide with or without IPL did not show a significant difference in comparison to using IPL alone. Dierickx et al. demonstrated a clearance rate of 72% at 6 months post therapy (37). IPL was combined with RF and results showed that the mean lesion count was reduced by 47%; it was suggested that this reduction was due to reduction in sebaceous gland size and decreased perifollicular inflammation. Their findings were based on post treatment skin biopsies (38). In comparison with other modalities, IPL has been found to be less effective than PDL, but more effective than blue or red light.

Photopneumatic therapy

Photopneumatic therapy (PPX) combines pneumatic energy and broadband light (400–1200 nm) encompassing the blue wavelength: 410 nm, which is the greatest wavelength for porphryin absorption. The suction acts to lift the contents of the dermis bringing them closer to the skin surface, thus making energy transfer more effective. The epidermis and therefore melanin in the epidermis is spread out and the photopneumatic treatment reduces adverse effects on the epidermis such as pigmentary changes (39). In addition, the suction applied due to negative pressure may help to rid comedones of their contents. The action of PPX therefore involves a combination of thermal- and vacuum-related mechanical effects. A number of studies have used this technology for the treatment of acne. Fifty-six patients with mild-to-severe acne were treated with PPX and were reported by Shamban et al. to have a 50% clearance of lesions after one session and 90% after four sessions (39). Omi et al. observed ultrastructural changes to the pilosebaceous unit after PPX treatments (40). Histologically, the authors were able to observe extrusion of comedone contents from the infundibulum and thermal injury to the bacteria and pilosebaceous apparatus, supporting the theory that PPX decreased sebaceous gland activity. No adverse effects were reported.

Gold and Biron demonstrated efficacy with PPX in seven patients treated with a total of four treatments at 3-week intervals (41). A larger study by Wanitphakdeedecha et al. involving 20 patients who were treated at 2-week intervals demonstrated modest improvement in acne lesion counts (42).

In a prospective, multicenter, clinical trial involving 41 patients with mild-to-moderate acne, Narurkar et al. reported a 69% reduction in the inflammatory component, in contrast to 41% reduction in the non-inflammatory component of the disease (43). There were no adverse effects caused by the treatment with mild discomfort and transient erythema being the most reported side-effects. In the author's experience, this treatment is effective in the mild-to-moderate cases of acne and in combination with topical therapy.

Discussion

The treatment of acne vulgaris often requires combination therapy and a tailored treatment regimen to each case. Despite advances in our understanding of the disease and the wide array of topical and systemic therapies available, in many cases the disease can still be resistant to medical therapy and hence light-based treatments may offer an alternative or act as adjuncts.

Light-based technologies can largely be based on their photothermal effect, predominantly on the sebaceous glands and their associated dermal vessels, or on their photochemical effects by targeting the coproporphyrins produced by *P. acnes* leading to cell death. The photochemical effects can be produced with or without the application of a photosensitizer such as ALA, although most of the current evidence points toward the PDT-mediated effects of therapy on acne. This is particularly the case when sustainable duration of the results is taken into consideration. Unfortunately, the side-effects with PDT appear to be the main limiting factor for their use in the treatment of acne in the majority of the cases.

Blue and red light therapies in the form of LEDs have shown efficacy, with the former exhibiting a photochemical effect and the latter a predominantly immunomodulator and anti-inflammatory effect in addition to some photothermal effects. These effects appear to be much more superior again when combined with a photosensitizer (i.e., PDT effect as opposed to LED alone).

IPL has shown to be effective with its broadband range having a combination of photochemical and photothermal effects, although again the studies have

Table I. Target chromophore of laser/light in the treatment of acne.

Target	Laser/Light device	Mode of action
P. acnes	UV, blue light, red light, blue/red light combination	Photochemical
Sebaceous glands	Infrared lasers (1064-nm Nd:YAG, 1320 nm, 1450 nm, 1540 nm), and PDT	Photothermal
Combination of *P. acnes* and sebaceous glands	KTP, PDL, IPL, and PDT	Photothermal and photochemical

shown that IPL combination with a photosensitizer is superior to IPL therapy alone. Furthermore, when compared against PDL, the latter showed a superior effect.

Studies using the PDL in acne also showed conflicting results, although evidence of TGF-beta upregulation has been shown but this does not appear to be sufficient in controlling the disease in many cases. Both PDL and IPL have a place in acne treatment today, particularly in the cases where it is associated with acne-induced facial erythema. This is similarly the case with the KTP laser.

Infrared lasers are less widely used nowadays in acne due to the associated pain and discomfort.

PPX is a relatively new technology in the treatment of acne and appears to be effective in mild-to-moderate cases combining both photochemical effects with mechanical extrusion of comedonal contents in addition to a mild photothermal effect.

Despite the large number of published studies utilizing light-based technologies in acne, the results show mixed results and firm conclusions are difficult to draw. Many studies were open-labeled or lacked optimal methodological qualities and involved a relatively small number of patients. Lack of objective assessment of outcome further contributes to the somewhat tempered enthusiasm for using this technology in acne treatment. Larger, randomized, controlled trials with clear objective outcome measures and consistently agreed settings (which vary hugely from the published studies) would be needed.Table I.

Conclusion

Laser-and light-based therapies may act as alternative treatments for patients who have not responded or are not suitable for medical therapy. The effects of light-based therapies rely on photochemical, photothermal, or the combination of both effects. For light-based therapies to be effective, ideally targeting both the *P. acnes* as well as the sebaceous glands appears to be the best approach. To date, most of the studies were underpowered or showed inconsistent results with relatively small number of patients involved. Optimal parameters are yet to be established. In the author's opinion, light-based therapies often offer very effective treatment when combined with medical therapies in selected patients.

Declaration of interest: The author reports no declarations of interest. The author alone is responsible for the content and writing of the paper.

References

1. Webster GF. Acne vulgaris. BMJ. 2002;325:475–479.
2. McGinley KJ, Webster GF, Leyden JJ. Facial follicular porphyrin fluorescence: correlation with age and density of Propionibacterium acnes. Br J Dermatol. 1980;102:437–441.
3. 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;142:973–978
4. Rai R, Natarajan K. Laser and light based treatments of acne. Indian J Dermatol Venereol Leprol. 2013;79:300–309.
5. Lloyd JR, Mirkov M. Selective photothermolysis of the sebaceous glands for acne treatment. Lasers Surg Med. 2001; 31:115–120.
6. Elman M, Slatkine M, Harth Y. The effective treatment of acne vulgaris by a high-intensity, narrow band 405–420 nm light source. J Cosmet Laser Ther. 2003;5:111–117.
7. Ashkenazi, H, Malik Z, Harth Y, Nitzan Y. Eradication of Propionibacterium acnes by its endogenic porphyrins after illumination with high intensity blue light. FEMS Immunol Med Microbiol. 2003;35:17–24.
8. Leyden JJ, McGinley KJ, Mills OH, Kligman AM. Propionibacterium levels in patients with and without acne vulgaris. J Invest Dermatol. 1975;65:382–384
9. Na JI, Suh DH. Red light phototherapy alone is effective for acne vulgaris: randomized, single-blinded clinical trial. Dermatol Surg. 2007;33:1228–1233
10. Seaton ED Mouser PE, Charakida A, Alam S, Seldon PM, Chu AC. Investigation of the mechanism of action of nonablative pulsed-dye laser therapy in photorejuvenation and inflammatory acne vulgaris. Br J Dermatol. 2006;155: 748–755.
11. Sami NA, Attia AT, Badawi AM. Phototherapy in the treatment of acne vulgaris. J Drugs Dermatol. 2008;7:627–632.
12. Baugh WP, Kucaba WD. Nonablative phototherapy for acne vulgaris using the KTP 532 nm laser. Dermatol Surg. 2005;31:1290–1296.
13. Yilmaz O, Senturk N, Yuksel EP, Aydin F, Ozden MG, Canturk T, Turanli A. Evaluation of 532-nm KTP laser treatment efficacy on acne vulgaris with once and twice weekly applications. J Cosmet Laser Ther. 2011;13:303–307.
14. Elman M, Lask G. The role of pulsed light and heat energy (LHE) in acne clearance. J Cosmet Laser Ther. 2004;6: 91–95.
15. Boineau DAS, Angel S, Auffret N, Dahan S, Mordon S. Treatment of active acne with an erbium glass (1.54 micron) laser. Lasers Surg Med. 2004;16:55.
16. Kassir MND, Newton D, Maris M, Euwer R, Servell P. Er: Glass (1.54 mm) laser for the treatment of facial acne vulgaris. Lasers Surg Med. 2004;34:s65.
17. Angel S, Boineau D, Dahan S, Mordon S. Treatment of active acne with an Er:Glass (1.54 microm) laser: a 2-year follow-up study. J Cosmet Laser Ther. 2006;8:171–176.
18. Bogle MA, Dover JS, Arndt KA, Mordon S. Evaluation of the 1,540-nm Erbium:Glass Laser in the Treatment of Inflammatory Facial Acne. Dermatol Surg. 2007;33:810–817.
19. Friedman PM, Jih MH, Kimyai-Asadi A, Goldberg LH. Treatment of inflammatory facial acne vulgaris with the

1450-nm diode laser: a pilot study. Dermatol Surg. 2004; 30:147–151.
20. Jih MH, Friedman PM, Goldberg LH, Robles M, Glaich AS, Kimyai-Asadi A. The 1450-nm diode laser for facial inflammatory acne vulgaris: dose-response and 12-month follow-up study. J Am Acad Dermatol. 2006;55:80–87.
21. Perez-Maldonado ART, Krejci-Papa N. The 1,450-nm diode laser reduces sebum production in facial skin: a possible mode of action of its effectiveness for the treatment of acne vulgaris. Lasers Surg Med. 2007;39:189–192.
22. Laubach HJ, Astner S, Watanabe K, Clifford J, Rius-Diaz F, Zurakowski D, Manstein D. Effects of a 1,450 nm diode laser on facial sebum excretion. Dermatol Surg. 2009;35: 1181–1187.
23. Uebelhoer NS, Bogle MA, Dover JS, Arndt KA, Rohrer TE. Comparison of stacked pulses versus double-pass treatments of facial acne with a 1,450-nm laser. Dermatol Surg. 2007;33:552–559.
24. Yeung CK, Shek SY, Yu CS, Kono T, Chan HH. Treatment of inflammatory facial acne with 1,450-nm diode laser in type IV to V Asian skin using an optimal combination of laser parameters. J Drugs Dermatol. 2009;8:239–241.
25. Bernstein EF. A pilot investigation comparing low-energy, double pass 1,450 nm laser treatment of acne to conventional single-pass, high-energy treatment. Lasers Surg Med. 2007;39:193–198.
26. Wang SQ, Counters JT, Flor ME, Zelickson BD. Treatment of inflammatory facial acne with the 1,450 nm diode laser alone versus microdermabrasion plus the 1,450 nm laser: a randomized, split-face trial. Dermatol Surg. 2006;32: 249–255.
27. Pollock B, Turner D, Stringer MR, Bojar RA, Goulden V, Stables GI, Cunliffe WJ. Topical aminolaevulinic acid-photodynamic therapy for the treatment of acne vulgaris: a study of clinical efficacy and mechanism of action. Br J Dermatol. 2004;151:616–622.
28. Riddle CC, Terrell SN, Menser MB, Aires DJ, Schweiger ES. A review of photodynamic therapy (PDT) for the treatment of acne vulgaris. J Drugs Dermatol. 2009;8:1010–1019.
29. Yeung CK, Shek SY, Bjerring P, Yu CS, Kono T, Chan HH. A comparative study of intense pulsed light alone and its combination with photodynamic therapy for the treatment of facial acne in Asian skin. Lasers Surg Med. 2007;39:1–6.
30. Rojanamatin J, Choawawanich P. Treatment of inflammatory facial acne vulgaris with intense pulsed light and short contact of topical 5-aminolevulinic acid: a pilot study. Dermatol Surg. 2006;32:991–996.
31. Taub AF. A comparison of intense pulsed light, combination radiofrequency and intense pulsed light, and blue light in photodynamic therapy for acne vulgaris. J Drugs Dermatol. 2007;6:1010–1016.
32. Hongcharu W, Taylor CR, Chang Y, Aghassi D, Suthamjariya K, Anderson RR. Topical ALA-photodynamic therapy for the treatment of acne vulgaris. J Invest Dermatol 2000;115: 183–192.
33. Goldman MP, Boyce SM. A single-center study of aminolevulinic acid and 417 NM photodynamic therapy in the treatment of moderate to severe acne vulgaris. J Drugs Dermatol. 2003;2:393–396.
34. Itoh Y, Ninomiya Y, Tajima S, Ishibashi A. Photodynamic therapy of acne vulgaris with topical delta-aminolevulinic acid and incoherent light in Japanese patients. Br J Dermatol. 2001;144:575–579.
35. Babilas P, Schreml S, Szeimies RM, Landthaler M. Intense pulsed light (IPL): a review. Lasers Surg Med. 2010;42: 93–104.
36. Lee EJ LH, Lim HK, Shin MK, Suh DH, Lee SJ, Kim NI. An open-label, split-face trial evaluating efficacy and safty of photopneumatic therapy for the treatment of acne. Ann Dermatol. 2012;24:280.
37. Dierickx CC. Treatment of acne vulgaris with a variable-filtration IPL system. Lasers Surg Med. 2004; 34:66.
38. Prieto VG, Zhang PS, Sadick NS. Evaluation of pulsed light and radiofrequency combined for the treatment of acne vulgaris with histologic analysis of facial skin biopsies. J Cosmet Laser Ther. 2005;7:63–68.
39. Shamban AT Enokibori M, Narurkar V, Wilson D. Photopneumatic technology for the treatment of acne vulgaris. J Drugs Dermatol. 2008;7:139–145.
40. Omi T, Munavalli GS, Kawana S, Sato S. Ultrastructural evidence for thermal injury to pilosebaceous units during the treatment of acne using photopneumatic (PPX) therapy. J Cosmet Laser Ther. 2008;10:7–11.
41. Gold M, Biron J. Efficacy of a novel combination of pneumatic energy and broadband light for the treatment of acne. J Drugs Dermatol. 2008;7:639–642.
42. Wanitphakdeedecha R, Tanzi EL, Alster TS. Photopneumatic therapy for the treatment of acne. J Drugs Dermatol. 2009;8:239–241.
43. Narurkar VA, Gold M, Shamban AT. Photopneumatic technology used in combination with profusion therapy for the treatment of acne. J Clin Aesth Dermatol. 2013;6: 36–40.