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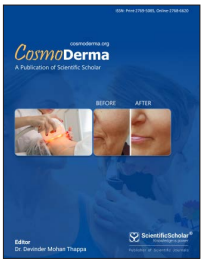

Review Article

Non-pharmacologic treatment for acne vulgaris

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ABSTRACT

Early rapid treatment of acne vulgaris is mandatory for improving the psychological behavior of acne patients and to avoid the occurrence of post acne scars that are still more frustrating and challenging condition in their treatment up till now. The current first line of treatment of acne vulgaris is the conventional pharmacological therapy including; keratolytics, topical or oral antibiotics, retinoids, and hormonal agents. Meanwhile, the use of this pharmacological therapy is not always beneficial because of poor compliance of the patients, occurrence of side effects of drugs and antibiotic resistance to *Cutibacterium (C.) acne* with high rate of recurrence. Therefore, non-pharmacological treatment is developed as safe and effective options for treating acne vulgaris. They are applied either as independent treatment modality, an adjunct to pharmacological therapy, or as maintenance therapy. There is no sufficient data on the classification of this treatment category. This review discusses the non-pharmacological therapy in management of acne vulgaris besides efficacy and safety of each type of treatment modality. The most commonly applied non-pharmacological therapies are diet control, counseling, dermocosmetics, comedo extraction, chemical peeling, cryotherapy, chemical peels, platelets rich plasma (PRP), botulinum neurotoxin A (BoNTA), light-based therapy and laser and photodynamic therapy (PDT). Regarding lasers and light sources, they can be subclassified according to their mechanism of action into devices targeting levels of *C. acnes*, function of the sebaceous unit, or both.

Keywords: Acne, Laser, Non-pharmacologic, Peeling, PDT, PRP

INTRODUCTION

Acne vulgaris ranks 8th in overall disease prevalence worldwide.[1] It affects approximately 85% of adolescents between 15 and 24 years old, however; it may appear firstly at 25 years or older in approximately 30% of all acne vulgaris. It is usually associated with social withdrawal and psychological impairment.[2] Its pathogenesis is multifactorial, although various mechanisms have been shown including; androgenic stimulation of sebaceous glands, altered follicular hyperkeratinization, obstruction of the pilosebaceous follicle, colonization with *Cutibacterium (C.) acnes* and inflammation.[3] There is up-regulation of some pro-inflammatory factors such as toll-like receptors (TLR), interleukin (IL)—1, IL-8, human β-defensin (hBD)—4, and matrix metalloproteinases.[4] Clinically, acne vulgaris is characterized by pleomorphic lesions, non-inflammatory (open and closed comedones) and inflammatory lesions (papules, pustules, nodules and cysts) in the areas that show the highest density of pilosebaceous unit (face, neck, back, shoulders, and upper chest).[5]

The current first line treatment for acne is conventional pharmacological modality as keratolytics, oral or topical antibiotics, retinoids and hormonal agents.[6] However, non-pharmacological therapies provide alternative, easy, effective and safe options for patients,[7] who find difficulty in adherence to traditional acne therapies or those who showed side effects or failure of conventional therapeutic treatment with antibiotic resistance.[6,8]

The most commonly non-pharmacological therapies are dietary control, counseling dermocosmetics, comedone extraction, chemical peels, cryotherapy, platelet rich-plasma (PRP), botulinum neurotoxin A (BoNTA), light-based therapies or laser and photodynamic therapy (PDT).[6,7,9–11]

DIETARY CONTROL

The relationship between incidence of acne and diet is still controversial. The main dietary factors, affecting acne vulgaris, are milk and dairy products, chocolate, glycemic load of diet, and dietary fiber.[12]

Milk and dairy products

Comedogenic effects of milk and dairy products are not yet conclusive. However, the probable cause of the comedogenic effects is the presence of insulin-like growth factor (IGF)—1 and hormonal content in the milk that is produced by cows during pregnancy. Important suggestions indicate that high intake of full-fat milk (≥ 2 glasses/day) are associated with moderate-to-severe acne with no significant relation to intake of semi-skimmed, skimmed dairy products or yogurt/cheese.[13,14] Meanwhile, Adilson and Thais[14] found that skimmed milk is more comedogenic than whole milk because of presence of hormonal imbalance (less estrogen) and changes of biologically active molecules (glucocorticoids, transforming growth factor [TGF]-β) during preparation of skimmed milk.

Chocolate

Slawson[15] found significant increase in acne lesions among adolescent students 48 hours after ingesting milk chocolate instead of jellybeans. However, dark chocolate is rich in antioxidants leading to smaller comedogenic effects.

Glycemic index

A high glycemic load diet may stimulate acne proliferation because of elevated insulin levels that increase secretion of androgens, sebum and IGF-1 that directly affect keratinocyte proliferation and apoptosis. Accordingly, ingestion of fast food and soda increase calories, carbohydrate, fat and glycemic load leading to acne lesions.[14]

Dietary fiber

In Kaufman study, acne patients consuming 30 gm/day high fiber breakfast cereal, showed significant improvement of their acne lesions.[16]

COUNSELING

Patient education about acne vulgaris is very important to increase knowledge and clinical outcomes and promote behavioral changes. This education can occur by traditional media (printed materials) and alternative multimedia (internet, educational website and digital video). It should reassuring that acne may improve as they get older with appropriate treatment, and the potential for permanent scarring decreases with early treatment.[17]

Patients must be educated about causes of acne, purpose of the medications prescribed and how to use them (orally and written instructions), the time frame for treatment to do its effect, to encourage adherence to treatment, the need for long-term maintenance therapy to prevent relapse and possible side effects and how to deal with them if occur. Patients should be advised to apply topical medications over the whole affected area not only the acne lesions to treat both visible lesions and microcomedones. Physicians, in turn, must tailor therapies to according to the patient's lifestyle, social status and financial circumstances.[18]

DERMOCOSMETICS

The use of dermocosmetics is recognized as an essential part of acne management. It can be used as either maintenance therapy or as complimentary to pharmacologic and light therapies for acne to decrease their adverse effects and can be formulated to target the main pathogenic factors of acne providing a synergistic effect.[19]

Types of dermocosmetic preparations

a-Moisturizers

Moisturizers can reduce skin dryness and irritation caused by some topical acne therapies and soothe the skin by reducing transepidermal water loss (TEWL). Moisturizers should be creams or gels (water and oily gels). Moreover, moisturizers containing ceramides would be effective in acne management because of reduction of skin surface ceramides in case of impaired skin barrier function with increased TEWL.[20]

b-Cleansers

Acne flare can occur by aggressive cleansing or by using cleanser with an alkaline pH, which can adversely affect skin barrier and microbiota, leading to irritation and inflammation.[19] Therefore, patients should be advised to wash acne skin areas with warm water and fingers using a cleanser with a pH between 5 and 7 for no more than twice daily.[21]

c-Camouflaging make-up

Camouflaging make-up can provide a quick solution to improve the appearance of acne lesions for enhancing the patient's quality of life. Acne patients are advised to use non-comedogenic cosmetics.[22]

d-Sunblock preparations

During summer months, ultraviolet (UV) exposure without any UV protection aggravates acne lesions because UVB rays cause thickening of stratum corneum, increase of sebum production and comedone formation and changes in skin microbiota. Therefore, the need for UV protection is mandatory in acne patients because of reduced skin barrier integrity leading to increased photosensitivity, which may be exacerbated by some preparations (e.g., retinoids).[23] Titanium dioxide is a common component in cosmetic formulations, such as compact cream foundations, and provides photoprotection by reflecting UV photons.[24]

Active ingredients in dermocosmetics for acne

a-Sebum controlling agents

Nicotinamide, an amide form of vitamin B3, is sebum-controlling and has anti-inflammatory properties to control acne, and may improve epidermal barrier permeability.[25]

b-Antimicrobial agents

Decanediol and tea tree oil are used as antimicrobial agents in dermocosmetics for acne. Therefore, decanediol reduced pustules and sebum levels during an 8-week treatment period in patients with mild-to-moderately severe acne. Tea tree oil reduced the severity of both inflammatory and non-inflammatory acne lesions.[26]

c-Anti-inflammatory agents

Salix alba, the active extract of willow bark, has an anti-inflammatory effect through decreased release of tumor necrosis factor (TNF)—α, cyclooxygenase (COX)—2, nitric oxide and IL-1b and IL-6.[27] Zinc, an anti-inflammatory agent, promotes wound healing. Clinically, zinc reduces the number of both acne lesions and seborrhea with no skin irritation.[28] Moreover, panthenol has anti-inflammatory properties and causes reduction of TEWL and increased intercellular lipid lamellae length, improving skin barrier function and hydration.[29] Probiotics may also be useful components in dermocosmetics as Lactobacillus plantarum has demonstrated both antimicrobial and anti-inflammatory properties resulting in modulation of skin microflora, repairing skin barrier, and reduction of skin erythema and size of lesions.[30]

d-Antioxidant agents

Antioxidants (e.g., epigallocatechin-3-gallate, Fullerene) have a role in treatment of acne as they have both anti-inflammatory effect and sebum controlling properties.[19]

COMEDONE EXTRACTION

It may help with treatment-resistant comedones and provide short-term reduction in the number of non-inflammatory lesions.[31]

CHEMICAL PEELS

Chemical peels include superficial type, which are comedolytic, exfoliating and anti-inflammatory. It has a role for management of non-inflammatory acne, but repeated sessions are needed in conjunction with a daily topical regimen. Also, they can improve post-inflammatory hyperpigmentation and skin texture.[32] Many studies investigated the efficacy of various chemicals in acne vulgaris[6]; beta-hydroxyl acid (salicylic acid 20–30%),[33-38] alpha-hydroxyl acid (glycolic acid, 10–70%),[36,37,39-41] Jessner solution,[33,34] trichloroacetic acid (TCA) 25%,[35] mandelic acid 10%,[37] amino fruit acid 20–60%,[41] and lipo-hydroxy acids 0.3–10%.[38] Most of these studies showed significant reduction in number of acne lesions after a predefined number of sessions[33-38,41] and reported no evident superiority when comparing those different types of chemicals[6] except two studies, who showed more significant improvement on non-inflammatory lesions with salicylic acid (30%) than with Jessner solution.[33,34] Two randomized, double-blinded, placebo-controlled researches with excellent methodological aspect reported strong evidence of efficacy on behalf of glycolic acid (10% and 40%).[39,40]

In general, chemical peels are safe despite occurrence of transient erythema, edema, dryness, desquamation, burning, itching and frosting. Temporary post-inflammatory hyperpigmentation was reported with the use of TCA, salicylic acid, and Jessner solution.[35]

CRYOTHERAPY

Cryotherapy using liquid nitrogen was effective against superficial lesions only. It is painful and causes stinging and burning for up to 4 hours.[42]

PLATELET-RICH PLASMA (PRP)

It is an autologous blood-derived product rich in platelets, chemokines, cytokines and growth factors (TGF, platelet-derived growth factor), IGF-1, and vascular endothelial growth factor that cause tissue remodeling and healing process by attraction of macrophages and increase collagen synthesis.[43,44] Additionally, it has an antibacterial role through presence of plasma proteins in platelet-poor plasma fraction (e.g., fibrinogen, prothrombin and fibronectin)[43] and antimicrobial peptides such as hBD-2 in PRP concentrate in addition to leukocyte action of white blood cells improving papulopustular and nodulocystic lesions.[43,45,46] Therefore, PRP demonstrated significant reduction in bacterial growth after 8 hours with more reduction after 24 hours for *Staphylococcus (S) aureus*, *S. epidermidis*, methicillin-resistant *S. aureus* and *C. acnes* compared with the whole-blood control group.[47] Also, hepatocyte growth factor has both anti-fibrotic and

anti-inflammatory actions that are mediated by disruption of transcription factor nuclear factor kappa B signaling, which acts as an inflammatory regulator besides its anti-inflammatory effects on COX-1, 2 and prostaglandin E2 production.[45]

Zhu *et al.*,[48] studying the efficacy of PRP in adjunct with ablative erbium fractional laser for management of facial acne scars, found that the already present acne lesions were cured in addition to absence of wounds after laser resurfacing, indicating that PRP has an advantage in regulating inflammation, increasing healing by inhibiting *C. acnes* and accelerating re-epithelialization and collagen remodeling. Recently, Moftah *et al.*[49] reported significant improvement of both non-inflammatory and inflammatory lesions in adolescents as well as post-adolescent patients after PRP therapy [Figure 1].

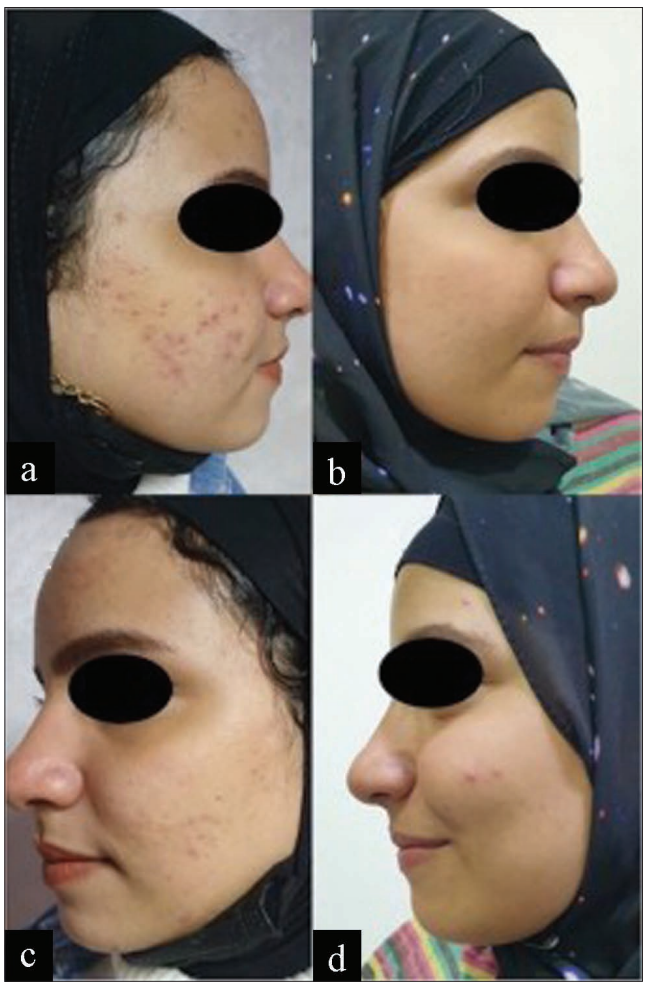

Figure 1: A 22-year-old female skin type IV: (a, b) PRP-treated side of the face (a, before treatment; b, after treatment). (c, d) Laser-treated side by 4 Nd:YAG treatment sessions (c, before treatment; d, after treatment). Clinical improvements are observed on both sides (Moftah *et al.*, 2022).[49]

BOTULINUM NEUROTOXIN TYPE A

Acne may result from an altered cholinergic response of pilosebaceous unit by increase acetylcholine (Ach) release, which causes sebum production and promotes keratinocyte adhesion, migration, differentiation and apoptosis by reaction of Ach with cholinergic receptors on keratinocytes` surfaces.[50] Moreover, acne severity correlates well with emotional stress because of role of adrenergic signaling for regulation of functional sebaceous glands. Upon a stress response, the body triggers neuropeptide secretion (substance P) and sympathetic–adrenomedullary axis to release catecholamines (epinephrine, norepinephrine, and dopamine), promoting sebum secretion with inflammatory reactions and proliferation of *C. acnes*.[51]

Botulinum neurotoxin A (BoNTA) can inhibit several pathogenic elements of acne development. Therefore, its intradermal injection can be performed to reduce sebum production and face oiliness by interfering with cholinergic transmission or adrenergic response by suppression of secretion of catecholamines and substance P.[11,51] Moreover, BoNTA can prevent formation of comedones through inhibition of adhesion of infundibular keratinocytes with better clearance of hair follicle opening.[11]

Clinically, improvement of perinasal acne was observed 1–2 weeks after injecting 20–25 units of onabotulinumtoxin A into the paranasal facial expression muscles with persistence of acne clearing up to 4 months.[52]

LASERS AND LIGHT SOURCES

Different light sources including; xenon, fluorescent, halogen, tungsten lamps and lasers, have been developed as more efficacious and safer treatment for acne vulgaris.[53] They work by decreasing levels of *C. acnes*, hypofunction of sebaceous unit or inflammation.[8,53,54] Among the devices approved by Federal Drug Administration (FDA) in United States and by regulatory bodies in European Union are blue light (approved in 2002); red light (approved in combination with blue in 2005); 1450 nm diode (approved in 2002); long pulsed-dye laser (PDL) (approved in 2004); and photopneumatic 400–1200 nm broadband light therapy (approved in 2007).[55]

Devices targeting *C. acnes*

C. acnes, the main pathogenic element in acne vulgaris, is a gram-positive microaerophilic cutaneous bacterium that produces endogenous porphyrins (uroporphyrin, protoporphyrin and coproporphyrin III), absorbing light energy at the near UV and blue light spectrum[56] Consequently, reactive free radical species released, leading to bacterial destruction as the singlet oxygen that

is a potent oxidizer destroying the lipids of cell wall of *C. acnes*. The most efficient wavelength lies between 400 and 430 nm, however, the reaction may be started with different wavelengths including; Potassium-titanyl-phosphate (KTP) lasers (532 nm), pulsed dye laser (PDL) (585–595 nm), intense pulsed light (IPL) devices (broadband light) and various orange/red lasers or light sources (610–635 nm).[57]

a- Blue light & combined blue-red light

Generally, the sensitivity of *C. acnes* is highest for shorter wavelengths (400 and 430 nm) and reduces with increasing wavelength (532–635 nm). Therefore, blue light has the most effective visible wavelength (407–420 nm band) for photoactivation of endogenous porphyrin component of *C. acnes*. However, it has poor skin penetration. In contrast, red light (633 nm) has an anti-inflammatory property by influencing cytokine release from macrophages besides its deeper penetration up to the level of sebaceous glands.[57,58] Several open label researches showed more improvement in inflammatory lesions of mild to moderate acne with combined blue-red light therapy than blue light alone[58] [Table 1].

b- UVA/UVB

Improvement of acne lesions was demonstrated in 70% of patients after sunlight exposure.[59] However, UVA and UVB rays affect acne differently. UVA rays, specifically UVA1 and blue light (400 nm) may have anti-inflammatory effects. In contrast, UVB rays cause inflammation, increase sebum production and proliferation of keratinocytes[23] [Table 1].

c-Photopneumatic therapy

Photopneumatic device is the only laser or light-based device approved by FDA for treatment of both non-inflammatory and inflammatory acne lesions. Using this device, a gentle vacuum is applied to skin surface leading to mechanical evacuation of both sebum and necrotic cells. Moreover, this device stretches the skin within the treatment tip, thereby reducing the concentration of competing chromophores such as hemoglobin and melanin so that the light can directly target the porphyrins in *C. acnes*. Therefore, mechanical extrusion of thermally injured bacteria as well as comedone contents can occur after treatment.[60]

Table 1: Phototherapy in acne (Charakida *et al*., 2004).[59]

Source of phototherapy	Treatment regimen	
	Duration	Dosage
Phototherapy UVA, UVB radiation	UVB continuous spectrum 280–340 nm and UVA 360 nm	Twice weekly for 8 weeks
Visible light	Cumulative dose 22 KJ/cm^2	17 irradiations
	Cumulative dose 325 J/cm^2	10 irradiations for 10 min
	UVA 380 nm, violet light 405 nm and 420 nm, and green light 395 nm	20 min, three times weekly for 7
Blue light	407–420 nm at 90 mW/cm^2	Twice weekly for 5 weeks
Combination of blue-red light	Red lamps 660 + 10 nm at 2.67 mW/cm^2, blue lamp 415 + 207-15 nm at 0.23 mW/cm^2	15 min daily for 12 weeks
Photodynamic therapy	20% ALA (for 3 hours) broad-band light 550–700 nm at 150	Weekly for 4 weeks J/cm^2
	20% ALA (for 4 hours) and pulsed excimer dye laser 635 nm at 5 J/cm^2	Once
	20% ALA (for 4 hours) and broadband halogen source. 600–700 nm at 17 mW/cm^2, total energy of 13 J/cm^2	Non stated
Laser	585 nm at 1.5 and 3 J/cm^2	Every 3 months

ALA: aminolevulinic acid

Devices targeting sebaceous glands

Therapies, which target the sebaceous gland with the goal of reduction in its size and sebum output, can show improvement of acne lesions.[57]

a-Infrared lasers

The infrared lasers (1450-nm Diode and 1540-nm Erbium Glass) have become the most effective acne treatment method. These lasers target water that is the dominant chromosphere in sebaceous gland, and selectively produce thermal heating and coagulation in upper to mid dermis where sebaceous glands are present causing decrease in sebum secretion, thereby eliminating acne.[57]

Diode Laser (1450-nm)

Jih *et al.*[61] performed three treatment sessions every 4–6 weeks using a fluence of 14 J/cm^2 and showed reduction of both sebaceous gland activity (measured by Sebutape scores) and inflammatory acne lesions, with long-term remission of 76.1% reduction up to 12 months after last session.

Erbium Glass Laser (1540-nm)

With the use of 1540-nm erbium glass laser in acne patients, Angel *et al.*,[62] who performed four sessions on active lesions of face and back every 4 weeks, demonstrated reduction in skin oiliness and long-term acne clearing by finding 71%, 79%, and 73% improvement of active lesions after 6 months, 1 year and 2 years, respectively.

b- Radiofrequency

Using the monopolar radiofrequency device, there is great reduction in inflammatory acne lesions after one session[63] because of reduction in perifollicular inflammation and sebaceous gland size. Temporary erythema, tingling and burning are the most common adverse effects.[57] Fractional

microneedling radiofrequency (FMRF) is a type of radiofrequency with insulated microneedles to deliver energy at the point of penetration up to the deep dermis without destruction of the epidermis, causing thermal damage to pilosebaceous unit and improvement of acne lesions.[64] One split-face randomized controlled trials (RCT) study reported significant reduction of 80% and 65% on both inflammatory and non-inflammatory acne respectively in favor of FMRF treatment side after two sessions with 4 weeks interval.[65]

There are different devices of FMRF, which are safe and effective in treatment of acne vulgaris, regarding the number of containing microneedle electrodes such as that containing 25 microneedles[66] and other having 49 microneedles.[64] Kim *et al.*[64] performed three sessions with 1 month interval using the device containing 49 microneedles and found reduction of sebum production and both types of acne lesions, especially inflammatory variant, at 1 and 3 months after last session, with significant reduction in these lesions compared with baseline.

Regarding side effects of FMRF, pain and temporary bleeding occurred frequently when the procedure was conducted with a depth of 1.5 mms, but rarely in superficial techniques. If the tip was removed rapidly, burns could occur due to current on the superficial epidermis, and postinflammatory hyperpigmentation could follow.[64] Moreover, erythema and swelling were severe after the procedure, but subsided within 1 week.[65]

c-1064 nm Long-Pulsed Neodymium:Yttrium-Aluminum-Garnet Laser (Nd: YAG)

The possible mechanism of 1064-nm long-pulsed Neodymium: Yttrium-Aluminum-Garnet (Nd: YAG) in treating acne lesions is derived from its deeper penetration into the dermis to selectively and thermally destroy the hyperactive sebaceous glands reducing the inflammatory acne lesions. Other mechanisms of action include reductions of some cytokines such as IL-8 (associated with epidermal hyperplasia) and TLR-2 (activated by *C. acnes*) and promoting healing process with collagen remodeling that is associated with increased cutaneous expression of TGF-β.[67]

Some studies, using 1064-nm Nd: YAG treatment, showed significant decrease of acne lesions up to complete clearance in some cases. Moreover, 1064-nm Nd: YAG treatment has a more sustainable effect and higher patient satisfaction with limited downtime than 595-nm PDL in treating acne lesions, especially in dark skin patients with self-limited side effects.[54,68] Recently, Moftah *et al.*[49] performed a split-face study comparing the efficacy of intralesional PRP injection versus 1064 nm long-pulsed Nd:YAG laser in both adolescents and post-adolescent patients with moderate acne vulgaris by doing four sessions, with 2 weeks interval. They found that both treatment methods are safe and effective for controlling both types of acne lesions in both adolescents and post-adolescent patients [Figure 2].

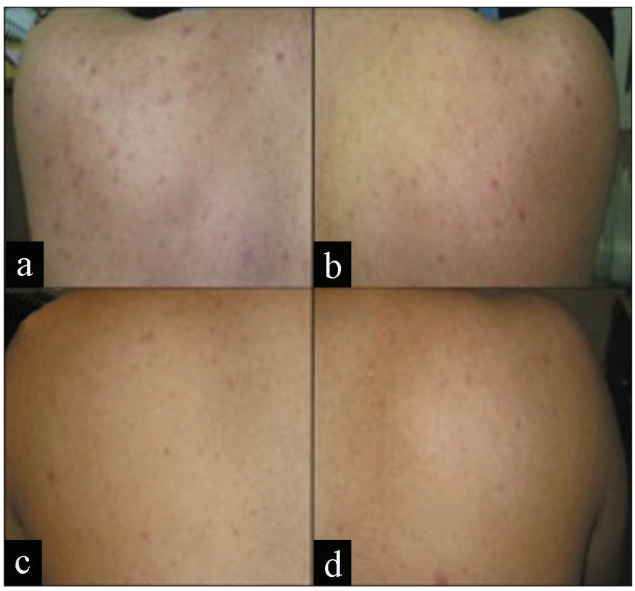

Figure 2: LMB-PDT side before and after treatment (a, b), IPL-treated side before and after treatment (c, d). Both sides of the face showed moderate improvement after three sessions 1 week in between (Moftah *et al.*, 2016).[78]

Target *C. acnes* and sebaceous gland

a-The 532 nm Potassium-titanyl-phosphate (KTP)

Green light has been tried as it has deeper penetration than the blue light and induces activation of porphyrins. It is well tolerated and causes non-specific thermal injury to sebaceous glands.[69] Therefore, some prospective split-face studies using 532 nm KTP laser showed improvement of lesions in mild to moderate acne at 1 month after four sessions with minimal side effects. Also, decrease in sebum production by 28% was detected, with little effect on *C. acnes* (measured by fluorescent photography).[70] Furthermore, Yilmaz *et al.*[71] confirmed the significant efficacy and safety of KTP in 38 acne vulgaris patients either with once (for 4 weeks) or twice weekly sessions (for 2 weeks).

b-Pulsed Dye Laser (PDL)

Pulsed dye laser produces photoxic effects on *C. acnes* through delivery of coherent yellow light and also targets oxyhemoglobin, causing selective photothermolysis of dilated vascular component of inflammation in acne.[72] Seaton *et al.*[73] reported 49% improvement of inflammatory acne lesions at 12 weeks after one treatment session using PDL versus 10% improvement in the controls, who were treated with a disconnected laser handpiece. This result may be explained by showing significant local anti-inflammatory actions through upregulation of TGF-β that is a potent inhibitor of inflammation and a potent stimulator of neocollagenesis without any effects on the degree of *C. acnes* colonization or sebum production as measured by the standardized application of absorptive tape.[74]

c-Intense pulsed light (IPL)

IPL source provides a non-coherent (400–1200 nm) source of intense light, which can be modified by filters to provide irradiation with specific wavelengths of light.[75] The reaction mechanism of the IPL sources is based on the principle of selective photothermolysis resulting in decreased gland size and reduced sebum production. In addition, it has an anti-inflammatory action through down regulation of TNF-α and upregulation of TGF-β.[76] Moreover, Barakat *et al.*[77] confirmed that IPL could improve acne lesions through targeting both sebaceous glands and inflammation by detecting significant decrease of surface area of sebaceous glands and inflammatory infiltrate respectively at 2 weeks after last session compared to baseline [Figure 3]. However, Moftah *et al.*[78] proposed another theory of cytotoxic effect on *C. acnes* through photoactivation of porphyrins that are produced by *C. acnes*, but it has no role on the sebaceous gland with the risk of recurrence due to bacteria regrowth.

The pulse duration of IPL is technically restricted to milliseconds (ms) range and should be lower than the thermal relaxation time of the target tissue to avoid damage of surrounding tissue. In addition to single pulses, higher fluences can be produced by using burst pulses, with 1 and 300 ms pulse interval, allowing the epidermis to cool down between the pulses while heat is maintained in the larger targets such as hair follicles or blood vessels.[79]

Mild to moderate acne patients, who were treated with IPL (430–1100 nm) twice weekly for 4 weeks, showed 74% and 79% reductions in inflammatory and non-inflammatory lesions respectively, at 1 month after eight treatment sessions.[80] After that, Barakat *et al.*[77] performed 6 IPL sessions with 2 weeks interval and detected significant decrease of total acne lesions especially inflammatory type [Figure 4]. Pigmentary changes (hypopigmentation or hyperpigmentation) might occur and persist longer or may even be irreversible. It can be mostly prevented by adjusting fluencies and wavelengths according to treatment area and patient's skin type.[80]

d-Photodynamic therapy (PDT)

PDT requires 3 factors including; a photosensitizer, oxygen and light. The most common photosensitizers are 5-aminolevulinic acid (ALA) or methylaminolevilunate in addition to the newer ones (Indocyanine green, Indole-3-acetic acid[81] and liposomal methylene blue [LMB]).[78] Sources of light are fluorescent lamps, light emitting diodes, IPL (filtered xenon flashlamps), filtered incandescent or arc lamps, sunlight and lasers[82] [Table 1].

PDT involves application of ALA, which is deposited in pilosebaceous units and metabolized through the heme synthesis pathway to produce protoporphyrin IX that is photoactivated with consequent release of singlet oxygen and free radicals producing cytotoxic actions on *C. acnes*

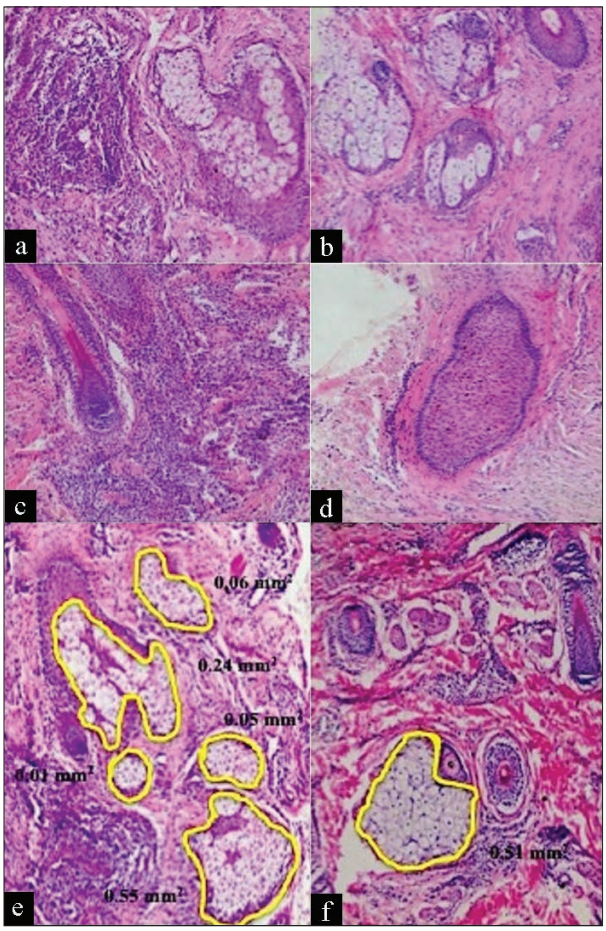

Figure 3: Skin biopsy specimens before and after IPL. The inflammatory infiltrate after IPL is significantly decreased (b, d, f) when compared to baseline biopsies (a, c, e). Histometry of skin biopsy specimens (e, f) showing significant decrease in surface area of sebaceous glands after IPL (f) when compared to baseline biopsies (e) (H&E; 3100) (Barakat *et al.*, 2017).[77]

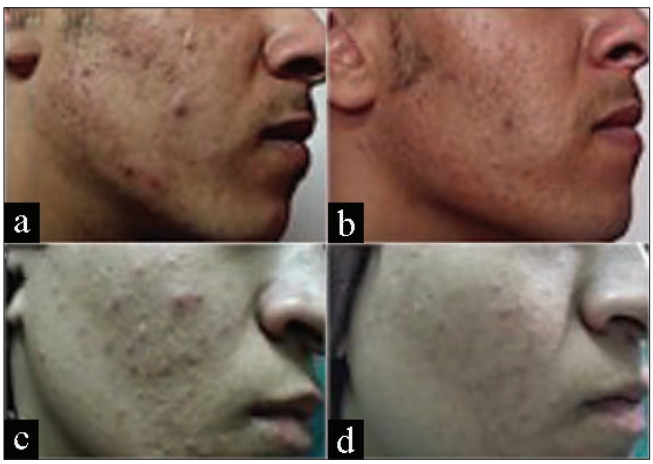

Figure 4: Clinical evaluation of acne vulgaris patients in response to IPL. Representative photographs of face (a–d) before (a, c) and after IPL (b, d) (Barakat *et al.*, 2017).)[77]

and damage to pilosebaceous unit. Several studies have utilized IPL after topical application of photosensitizer.[57,78] Moftah *et al.*[78] found that both IPL alone and IPL (550-nm cut-off filter) with PDT by LMB once weekly for three sessions showed significant decrease in the numbers of both non-inflammatory and inflammatory lesions, but LMB-IPL is more effective than IPL alone. Adverse effects of PDT include edema, erythema, blistering, acneiform eruptions and hyperpigmentation.[78]

In conclusion, our review discussed several non-pharmacological therapies such as dietary control, counseling, dermocosmetics, comedone extraction, chemical peels, cryotherapy, PRP, BoNTA, light-based therapies or laser, and PDT. Regarding lasers and light sources, this review modified their classification according to their mechanism of action into devices targeting levels of *C. acnes*, function of the sebaceous unit or both. On reviewing the literature, there is growing increase in the number of studies performed in the area of non-pharmacological therapy of acne, and the need for conclusive evidence for the effective non-pharmacological treatment options for acne emphasizes using double-blinded placebo-controlled study designs.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Nil.

Conflict of interest

Prof. (Dr.) Nayera Hassan Moftah is on the Editorial Board of the journal.

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