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Intense pulsed light versus benzoyl peroxide

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ABSTRACT

The intense pulsed light (IPL) therapy has three mechanisms of action in acne vulgaris: photochemical, photoimmunological, and photothermal. In this clinical trial, 47 patients with facial inflammatory acne lesions, ages ranging from 15 to 40 years, were enrolled. Patients were categorized into two groups: (a) 20 patients in Group A treated with IPL for 3 sessions, 3 weeks apart, (b) and 27 patients in Group B treated with benzoyl peroxide (BPO) 2.5% gel daily at night for 9 weeks. Follow up was done at 3 weeks after the end of treatment. The effect of treatment was evaluated objectively according to total lesion counting and digital photographic assessment and subjectively according to the patients' satisfaction. IPL is an effective and well-tolerated method for the treatment of inflammatory facial acne like BPO. Therefore, the IPL can be used as a standard therapy for inflammatory acne vulgaris.

Keywords: *clinical trial; facial acne; Iraqi patients; objective; pulsed light; subjective; vulgaris*

INTRODUCTION

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit that affects more than 85% of adolescents and young adults.[1] The clinical lesions are noninflammatory, closed, and open comedones and/or pustules, papules, and nodules of variable degrees of inflammation and depth. The most frequently affected locations are the face and back and/or chest. Postinflammatory hyperpigmentations and scarring occur commonly.[2]

Acne is regarded to be on top of the three most common diseases.[3] Acne can be present at birth as neonatal acne and infantile acne (presents between 1 and 12 months) and extending into adulthood. Acne

can persist from adolescent period into adulthood or may start after the adolescence.[4] The adrenarche age appears to be dropping over the years, so acne may present at an earlier age. The acne severity may also be genetically determined.[5] In twin studies, 81% of the population variance in acne was found to be due to genetic factors, while 19% was due to environmental factors.[6,7]

Follicular hyperkeratinization

Corneocytes are normally shed into the lumen of the follicle. There is an increase in corneocyte cohesiveness and follicular keratinocyte proliferation, which leads to the development of a hyperkeratotic plug. There are data supporting the role of interleukin-1α (IL-1α) as inciting factor for microcomedo formation.[8] The plug enlarges behind a very small follicular opening and become visible as closed comedone (whitehead). An open comedone (blackhead) occurs if the follicular orifice dilates. Closed comedone is the precursor of inflammatory acne papules, pustules, and cyst.[9]

Hormonal factor

At adrenarche, circulating levels of dehydroepiandrosterone sulfate (DHEAS) begin to increase by the adrenal gland. The rise in DHEAS serum levels in prepubertal children is associated with an increase in sebum production.[7] Preadolescent acne is due to urinary excretion of androgenic steroids and rise in sebum production.[10]

Pilosebaceous unit either synthesize androgens *de novo* from cholesterol or locally by converting circulating weak androgens to more potent ones. Testosterone can be activated to physiologically more potent tissue androgen 5α-dihydrotestosterone (5α-DHT) by the effect of 5α-reductase.[11] Type I 5α-reductase is mainly found in the sebocytes, keratinocytes, and fibroblasts. It enhances sebum production by local production of DHT. Newly found type III 5α-reductase may also play a role in regulating sebum production.[12] DHT can induce follicular keratinocytes proliferation.[4]

Inflammation

The clinical lesion that can be seen is determined by the type of inflammatory response. Suppuration occurs, and a pustule is formed if neutrophils predominate (early lesions). Neutrophils can also facilitate the inflammatory response by generating reactive oxygen species (levels in the skin and plasma may correlate with acne severity) and releasing lysosomal enzymes.[13]

Increased expression of proinflammatory mediators

1. Upregulation of inflammatory mediators in early lesions and uninvolved skin (E- selectin, integrin, vascular adhesion molecule-1, and IL-1).[14]
2. IL-1α bioactivity in open comedones, and elevation of macrophages and CD3+ and CD4+ T cells in uninvolved skin.[14]
3. Upregulation of defensin-2 immunoreactivity.[15,16]

Toll-like receptors (TLRs): Activation by *Propionibacterium acnes* triggers inflammatory cytokines responses.[17]

Microorganism

P. acnes is regarded to be a commensal organism of the skin rather than a pathogen.[18] The pathogenicity of *P. acnes* includes stimulation of keratinocytes and inflammatory cells to produce proinflammatory mediators and reactive oxygen species, as well as the direct release of chemotactic factors, lipases, and enzymes, that contribute to comedo rupture.[7] One mechanism is via TLRs; TLR2, which recognizes peptidoglycans and lipoproteins as well as Christie–Atkins–Munch–Peterson (CAMP) factor 1 produced by inflammatory strains of *P. acnes*, is present on the surface of macrophages that surround acne follicles.[19,20] By activation of the TLR2 pathway, *P. acnes* stimulates the release of proinflammatory mediators such as IL-1α, IL-8, IL-12,

tumor necrosis factor-α (TNF-α), and matrix metalloproteinases.[17,20,21]

P. acnes can activate the NOD-like receptor protein 3 (NLRP3) of inflammasomes in the cytoplasm of both monocytes and neutrophils, resulting in proinflammatory IL-1B release.[22] Recent studies have shown that *P. acnes* can also stimulate T-helper 17 responses in acne lesions.[23] During their growth and proliferation in the follicular units, *P. acne* can produce protoporphyrin IX and coproporphyrin III by absorbing light in the near ultraviolet and visible light with the major peak of absorption at 415 nm, and this will form singlet oxygen which leads to destruction of the bacteria.[24] Lastly, *P. acnes* can induce monocytes to differentiate into two innate immune cell subsets: (a) CD1b+ dendritic cells activating T cells to release proinflammatory cytokines; and (b) CD209+ macrophages, which effectively phagocytose and kill *P. acnes*.[25]

The aim of this study is to evaluate the efficacy of intense pulsed light therapy (IPL) versus benzoyl peroxide (BPO) 2.5% gel in treatment of mild to moderate inflammatory facial acne vulgaris.

IPL device: Quanta system DNA laser technology (made in Italy).
Crystal shape and size: Rectangular shape, 48 mm× 13 mm^2.
Wavelength: 400 nm.
Pulse duration: 8 ms.
Fluence: 8–11 J/cm^2.

FIGURE 1. IPL device.

PATIENTS AND METHODS

Patients were collected from outpatient clinic at Al-Sadr Medical City in Najaf City, Iraq during the period between April 2019 and February 2020.

Study design

This study was a clinical trial for the evaluation of effectiveness of the IPL 400 nm versus BPO 2.5% gel in treatment of mild to moderate inflammatory facial acne vulgaris in Iraqi patients.

Specifications of the IPL device used in the study is shown in figure 1.

Patient selection

Forty-seven patients (20 patients treated with IPL, Group A, and 27 patients treated with BPO gel 2.5%, Group B) with inflammatory acne lesion on the face and Fitzpatrick skin phototype II and III were included in this study. They were recruited from the outpatient clinic. All patients had mild to moderate acne lesions, and their ages ranged from 15 to 40 years.

Inclusion criteria

Inclusion criteria include:

- Patients with mild to moderate inflammatory facial acne vulgaris.
- Patient preference to experience laser therapy.

Exclusion criteria

Exclusion criteria include:

- Skin phototype IV, V, and VI.
- Severe inflammatory acne.

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- Patients receiving topical or systemic antibiotic in the last 2 weeks.
- Patients receiving systemic steroid and retinoid in the last 6 months.
- Photosensitivity.
- Hypersensitivity to BPO.
- Pregnant patients or patients who are breastfeeding.
- Tendency to develop hypertrophic and keloid scars.
- Irregular visits or loss to follow-up.

RESULTS

Of the 47 patients (20 patients treated with IPL, Group A, and 27 patients with BPO 2.5% gel, Group B) enrolled in the study, 40 patients completed the treatment and follow-up period of the study, and 7 patients from Group B dropped out for different reasons. Their ages ranged from 15 to 40 years with mean ± SD of 22.725 ± 5.652. The disease duration varied between 6 months and 7 years with mean ± SD of 3.880 ± 1.860. There is no significant difference in age (P value = 0.721) and duration (P value = 0.664) of disease for both groups. There were 10 (25%) male patients; 5 (12.5%) of them were included in Group A, and the remaining 5 (12.5%) males were included in Group B. Of the 30 (75%) female patients, 15 (37.5%) of them were included in Group A, and the remaining 15 (37.5%) were included in Group B. According to Fitzpatrick classification for skin types, 10 (25%) patients were of skin type II; 5 (12.5%) patients were included in Group A, and 5 (12.5%) patients were included in Group B. Thirty (75%) patients were of skin type III; 15 (37.5%) patients were included in Group A, and 15 (37.5%) patients were included in Group B.

The severity of acne lesions was graded according to TLC. Ten (25%) patients were graded as mild, 5 (12.5%) patients were included in Group A, and 5 (12.5%) patients were included in Group B, while 30 (75%) patients were of moderate severity, 15 (37.5%) patients were included in Group A and 15 (37.5%) patients were included in Group B. The association between type of treatment and gender, phototype, and severity is shown in Table 1.

The gender distribution, phototype, and severity of disease in both study groups show no significant difference as shown in Table 1.

Evaluation

The improvement in the condition of the patients after treatment sessions was evaluated as follows:

Objective methods

Total lesion counting: The mean ± SD total lesion count (TLC) value before IPL treatment was 24.950 ± 9.087, while for BPO treatment the group mean ± SD TLC value before treatment was 24.050 ± 6.855. Thus, the difference was statistically not significant, P value = 0.726.

At the follow-up visit, the mean ± SD TLC value for Group A was 10.950 ± 5.195, while for Group B, the mean ± SD TLC value was 10.700 ± 6.408, so the difference was statistically not significant, P value = 0.893. TLC showed no significant difference between both study groups in all visits (Table 2).

While in the same group, there is statically significant difference before and after treatment for both groups with improvement in inflammatory lesions by 55.5%, P value < 0.001 in each group (Table 3).

At the end of the study, most of the patients still had a few newly occurring lesions despite healing of most old acne lesions.

Photographic assessment: There is no significant difference between both groups when evaluated using photographic assessment (Table 4).

The mean visual analog scores for the two assessors showed no significant difference in both study groups, P value = 0.494 (Table 5).

Subjective methods

Patient satisfaction: At baseline visit, all patients who were not satisfied were regarded as 0. According

TABLE 1. Association between Type of Treatment and Gender, Phototype, and Severity.

		Groups		Total	P value
		A	B		
Gender	Male	5 (12.5%%)	5 (12.5%)	10 (25.0%)	1
	Female	15 (37.5%)	15 (37.5%)	30 (75.0%)	
Phototype	PII*	5 (12.5%)	5 (12.5)	10 (25.0%)	1
	PIII*	15 (37.5%)	15 (37.5%)	30 (75.0%)	
Severity	Mild	5 (12.5%)	5 (12.5%)	10 (25.0%)	1
	Moderate	15 (37.5%)	15 (37.5%)	30 (75.0%)	
Total		20 (50.0%)	20 (50.0%)	40(100.0%)	

**P, Phototype.*

TABLE 2. Total Lesion Count in Both Study Groups.

	Groups	Mean	SD	P value
TLC1	A	24.950	9.087	0.726
	B	24.050	6.855	
TLC2	A	15.750	7.246	0.654
	B	16.750	6.750	
TLC3	A	12.900	6.398	1
	B	12.900	5.505	
TLC4	A	10.950	5.195	0.893
	B	10.700	6.408	

SD, standard deviation; TLC, total lesion count.

TABLE 3. Total Lesion Count Before and after for Each Group.

		Mean	SD	P value
A	TLC 1	24.950	9.087	<0.001
	TLC 4	10.950	5.195	
B	TLC 1	24.050	6.855	<0.001
	TLC 4	10.700	6.408	

SD, standard deviation; TLC, total lesion count.

TABLE 4. Photographic Assessment in Both Study Groups.

		Groups		P value
		A	B	
Photographic assessment	Poor	1 (5%)	0 (0%)	0.605
	Fair	3 (15%)	5 (25%)	
	Good	8 (40%)	9 (45%)	
	Excellent	8 (40%)	6 (30%)	
Total		20 (100%)	20 (100%)	

to this method, mean ± SD for Group A patient satisfaction after the first treatment (Visit 2) was 3.900 ± 1.552, and for Group B patient satisfaction, mean ± SD was 2.650 ± 1.755, with P value = 0.022.

At follow-up visit (v4), mean ± SD was 6.000 ± 2.427 and 5.400 ± 1.788 for Groups A and B, respectively, with P value = 0.379. There was a significant difference with superiority to IPL group only after first session of treatment. The subsequent visits showed no significant difference (Table 6).

While in the same group there is statically significant difference before and after treatment for

TABLE 5. Mean Visual Analog Score for Both Study Groups.

	Groups	Mean	SD	P value
VAS	A	0.663	0.202	0.494
	B	0.621	0.176	

SD, standard deviation; VAS, visual analog score.

TABLE 6. Patient Satisfaction for Both Study Groups.

	Groups	Mean	SD	P value
V2	A	3.900	1.552	0.022
	B	2.650	1.755	
V3	A	5.050	2.038	0.269
	B	4.400	1.602	
V4	A	6.000	2.427	0.379
	B	5.400	1.788	

SD, standard deviation.

both groups, with P value = 0.000 in each group (Table 7).

At the end of the study, improvement in skin texture and skin getting smoother were noted in eight (20%) patients using IPL therapy. About four patients (10%) in Group A and six patients (15%) in Group B still had a few new occurring lesions regardless of healing of most old lesions.

DISCUSSION

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit developed due to the interplay of multiple factors including the hormonal effect on sebum composition and production and inflammation, mediated by *P. acnes*.[7]

BPO has lipophilic ability. Thus, it can penetrate the pilosebaceous duct, and it has been proved to be effective in superficial inflammatory acne. When applied on the skin, BPO decomposes to release oxygen free radicals, which has a bactericidal effect on sebaceous follicles as well as act as an anti-inflammatory agent.

TABLE 7. Patient Satisfaction Before Treatment and at Follow Up for Each Group.

		Mean	SD	P value
A	Patient sat. V1	0.00	0.000	0.000
	Patient sat. V4	6.00	2.427	
B	Patient sat. V1	0.00	0.000	0.000
	Patient sat. V4	5.40	1.788	

SD, standard deviation.

Technology of IPL was developed as an alternative treatment for acne vulgaris because of its effectiveness in accelerating the photochemical reaction of porphyrin, ability to decrease the risk of bacterial resistance, and faster onset of action.

At the end of the study, both IPL and BPO showed significant difference in therapeutic results, P value < 0.001, with improvement of inflammatory lesions by 55.5% for both treatment groups. At follow-up visit, there was no significant difference between the two groups, P value = 0.893.

CONCLUSIONS

The results of this study suggest that the IPL is an effective and well-tolerated method in the treatment of mild to moderate inflammatory facial acne like BPO. All patients were satisfied with the treatments, with no significant difference between both kinds of therapy.

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