**Efficacy of “Intense Pulsed Light versus Benzoyl Peroxide 2.5% Gel” in Treatment of Mild to Moderate Facial Acne Vulgaris in Iraqi patients**

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**Abstract:**

The Intense pulse light (IPL) therapy has three mechanisms of action in acne vulgaris; photo-chemical, photo-immunological and photo-thermal. In this clinical trial forty seven patients with facial inflammatory acne lesion , their ages ranged from 15 to 40 years were enrolled. Patients included in two groups, 20 patients in group A treated with IPL for 3 sessions; 3 weeks apart, and 27 patients in group B treated with BPO 2.5% gel daily at night for 9 weeks. Follow up at 3 weeks after the end 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 effective and well tolerated method in the treatment of inflammatory facial acne like BPO. Therefore, the IPL can be used as standard therapy for Inflammatory acne vulgaris.

**Keywords:** Pulsed light, subjective, objective, clinical trial, facial acne, vulgaris, Iraqi patients

1. **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 non-infammatory closed and open comedones and/or pustules, papules and nodules of varible degrees of inflammation and depth. The most frequently affected locations are the face, back and/or chest. Post-inflammatory hyperpigmentations and scarring commonly occur(2).

Acne is regarded to be on the top of three most common disease (3). Acne can present at birth with 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 due to genetic factors versus 19% environmental factors(6, 7).

**Follicular hyperkeratinization:**

Corneocytes are normally shed into the lumen of the follicle. There is increases in corneocyte cohesiveness and follicular keratinocyte proliferation, which leads to the development of a hyperkeratotic plug. Data support a role for 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 (black head) 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 raise 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-DHT by the effect of 5α-reductase(11) . Type I 5α-reductase 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 determined by the type of infammatory response. Suppuration occurs and a pustule is formed if neutrophils predominate (early lesions). Neutrophils also can 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. Up regulation 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, elevation of macrophages and CD3+ and CD4+ T cells in uninvolved skin(14).
3. Up regulation of defensin-2 immunoreactivity(15, 16).

**Toll- like receptors (TLRs):** Activation by *P. 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 Toll-like receptors (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 proinflammatory mediators release like 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* also can stimulates 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 absorbing light in the near ultraviolet and visible light with the major peak of absorption at 415 nm, this will form singlet oxygen leads to destruction of the bacteria (24). Lastly, *P. acnes* can induce monocytes to differentiate into two innate immune cell subsets: (**1**) CD1b+ dendritic cells activating T cells to release proinflammatory cytokines; and (**2**) CD209+ macrophages, which effectively phagocytose and kill *P. acnes*(25).

 The aim of the present work is to evaluate the efficacy of intense pulsed light therapy versus benzoyl peroxide 2.5% gel in treatment of mild to moderate inflammatory facial acne vulgaris.

1. **Patients and Methods**

Patients collected from out-patient clinic in Al-Sadr Medical City in Najaf city- Iraq during the period between April 2019 to 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:**

**IPL device:** Quanta system DNA laser technology ( made in Italy).

**Crystal shape &size:** rectangular shape, 48 mm\* 13 mm2.

**Wavelength:** 400 nm.

**Pulse duration:** 8 ms.

**Fluence:** 8- 11 J/cm2.

**Figure (2): IPL device**

**Patient selection:**

 Forty seven patients (20 patients treated with IPL; group A and 27 patients 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 have mild to moderate acne lesions, their ages ranged from 15 to 40 years.

**Inclusion criteria:-**

**Inclusion criteria includes:**

-Patients with mild to moderate inflammatory facial acne vulgaris.

-Patient preference to experience laser therapy.

**Exclusion criteria:-**

**Exclusion criteria includes:**

-Skin phototype IV, V and VI.

-Severe inflammatory acne.

-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.

-Patients have pregnancy or breast feeding.

-Tendency to develop hypertrophic and keloid scars.

-Irregular visits or loss to follow up.

1. **Result**

 Forty seven patients (20 patients treated with IPL; group A and 27 patients with BPO 2.5% gel; group B). Forty patients completed the treatment and follow-up period of the study. Seven 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 included in group A and 5 (12.5%) males included in group B while 30 (75%) female patients, 15 (37.5%) of them included in group A and 15 (37.5%) females included in group B. According to Fitzpatrick classification for skin types, 10 (25%) patients were of skin type II, 5 (12.5%) patients included in group A and 5 (12.5%) patients included in group B while 30 (75%) patients were of skin type III, 15 (37.5%) patients included in group A and 15 (37.5%) patients included in group B.

 The severity of acne lesions graded according to TLC, 10 (25%) patients graded as mild, 5 (12.5%) patients included in group A and 5 (12.5%) patients included in group B while 30 (75%) patients were of moderate severity, 15 (37.5%) patients included in group A and 15 (37.5%) patients included in group B. The association between type of treatment and gender, phototype and severity shown in table (2).

**Table (2): 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 |

 The gender distribution, phototype , and severity of disease in both study groups show no significant difference as shown in table 2.

**Evaluation:**

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

**A-Objective methods:**

**1-Total lesion counting:**

 The mean ± SD TLC value before IPL treatment was 24.950 ± 9.087 while for BPO treatment group mean ± SD TLC value before treatment was 24.050 ± 6.855, so 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 mean ± SD TLC value was 10.700 ± 6.408, so the difference was statistically not significant, P value= 0.893. Total lesion count show no significant difference between both study groups in all visits. Table (3)

**Table (3): 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 |

 While in the same group there is statically significant difference before and after treatment for both groups with improvement of inflammatory lesions by ( 55.5%), P value <0.001 in each group. Table (4)

**Table (4): 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 |

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

**2-Photographic assessment:**

 There is no significant difference between both groups regarding photographic assessment. Table (5)

**Table (5): 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%) |  |

 The mean visual analogue scores for the two assessors shows no significant difference in both study groups with P value= 0.494. Table (6)

**Table (6): Mean visual analogue score for both study groups.**

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

**B-Subjective methods:**

**-Patient satisfaction**

 At baseline visit , all patients not satisfied regarded as (0). According 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 group A, B respectively with P value= 0.379. There is significant difference with superiority to IPL group only after first session of treatment. In the next visits show no significant difference. Table (7)

**Table (7): 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 |

While in the same group there is statically significant difference before and after treatment for both groups with P value= 0.000 in each group. Table ( 8)

**Table (8): 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  |

At end of study, improvement in skin texture getting smoother is noted by eight ( 20%) patients in this study by using IPL therapy. About four patients (10%) in group A and six patients (15%) in group B still have few new occurring lesions regardless of healing of most old lesions.

1. **Discussion**

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit developed due to interplay of a 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 into 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 an anti-inflammatory agent.

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 it has faster onset of action.

 At the end of 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 is no significant difference between two groups, P value= 0.893.

1. **Conclusions**

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

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