

## Phototherapy versus Adapalene 0.1% Gel in Treatment of Acne Vulgaris

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### Abstract

**Background:** Phototherapy has been increasingly used for treatment of acne vulgaris. The targets of the action mechanism of each light treatment are generally thought to be *P. acnes*. Visible light has been proposed to work by decreasing *P. acnes* bacterial counts by activating endogenous porphyrins.

**Objective:** To evaluate the effectiveness of phototherapy with Pulsed Light and Heat Energy (LHE) versus topical Adapalene 0.1% in the treatment of mild forms of acne.

**Method:** During the period of 2 years were treated 99 patients with Acne vulgaris, 51 with mild form of Acne vulgaris were treated with Phototherapy and 48 patients with mild form were treated with topical Adapalene 0.1%. The effectiveness was based on the number of inflammatory and non-inflammatory elements in the beginning moment of therapy and in the intervals after two sessions, 4 sessions, 6 sessions, 8 sessions, one month after treatment with Phototherapy and after 2, 4, 6, 8, 10, 12 weeks treatment with Adapalene 0.1% Gel.

**Results:** One month after the treatment with Phototherapy, the inflammatory and non-inflammatory elements cleaning reached  $67.9 \pm 6.2\%$  in mild form and  $68.4 \pm 6.5\%$  in moderate form of Acne vulgaris. Three months after the treatment with local treatment, the inflammatory and non-inflammatory elements cleaning reached  $59.4 \pm 5.8$  in mild form and  $71.4 \pm 7.2$  after treatment with local plus systemic in moderate form of Acne vulgaris.

**Conclusion:** The treatment of Acne vulgaris with phototherapy LHE as mono-therapy is a medical alternative which gives good clinical results in a relatively short period of time (one month) and with minimal side effects.

**Keywords:** Wavelength; Phototherapy; Acne vulgaris; Cell membrane

### Introduction

Acne vulgaris is the most common disease and is characterized by non-inflammatory, open or closed comedones and by inflammatory papules, pustule and nodules. Acne vulgaris affects the areas of skin with the densest population of sebaceous follicles. These areas include the face, the upper part of the chest and the back.

### The pathophysiology of acne involves four key mechanisms of action

Abnormal proliferation and differentiation of keratinocytes, increased sebum production, hyper proliferation of Propionibacterium acnes, and an inflammatory response initiated by bacterial antigens and cytokines [1]. Acne vulgaris affects the areas of skin with the density of population of sebaceous follicles. These areas include the face, the upper part of the chest and the back *P. acnes* are an anaerobic organism present in acne lesions [2]. The presence of *P. acnes* promotes inflammation through a variety of mechanisms. *P. acnes* stimulates inflammation by producing pro-inflammatory mediators that diffuse through the follicle wall [3-8].

Studies have shown that *P. acnes* activate the toll-like (TL) receptor 2 on monocytes and neutrophils. Activation of the TL receptor 2 then leads to the production of multiple pro inflammatory cytokines, including interleukins (IL) and IL8 and tumor necrosis factor (TNF). Hypersensitivity at *P. acnes* may also explain why some individuals develop inflammatory acne vulgaris while others do not [9].

Inflammation may be a primary phenomenon or a secondary phenomenon. Most of the evidence to date suggests a secondary inflammatory response to *P. acnes* [4,5]. However, IL-alpha expression has been identified in microcomedones and it may play a role in the development of acne [7]. *Propionibacterium acnes* are an obvious target for acne phototherapy since it is central to the inflammatory process [1].

*P. acnes* makes porphyrins, which are present in the follicle, in proportion to its population. Once the porphyrins are exposed to visible light, it becomes chemically active and transfers to an excited state, resulting in the formation of singlet oxygen, which combines with cell membranes to destroy the *P. acnes*.

This process is depended on the rate of production of excited porphyrin molecules, which is influenced by the concentration of porphyrins, the concentration of photons, the temperature, and the wavelength of photons [1].

## Objective

The objective of this study is to compare the clinical efficacy of Phototherapy (LHE) versus Adapalene 0.1 Gel in the treatment of Acne Vulgaris.

## Method

During the period of 2 years were treated 99 patients with Acne vulgaris, 51 with mild form of Acne vulgaris were treated with Phototherapy and 48 patients with mild form were treated with topical Adapalene 0.1% Gel.

**For acne classification we used a recent proposal by the US FDA for a five-category global system. In this scale, the five categories ranged from**

- Clear, indicating no inflammatory or non-inflammatory lesions.
- Almost clear, rare non-inflammatory lesions with no more than one papules/pustule.
- Mild, some non-inflammatory lesions, no more than a few papules or pustules but no nodules.
- Moderate, up to many non-inflammatory lesions, may have some inflammatory lesions, but no more than one small nodule.
- Severe, up to many non-inflammatory and inflammatory lesions, but no more than a few nodules.

The continuous variables were presented through mean value and standard deviation and the categorical variables were presented in absolute and in percentage value. Continuous variables were compared through the Student's t-test and one-way ANOVA, which is used when more than two groups are compared. The Chi-square test was used for analysing the differences between the categorical variables. A p value less than <0.05 is considered significant.

In the first group, the study included the total of 51 patients treated with phototherapy at average age  $18.06 \pm 3.33$  years, 62.7% of whom were female and 37.3% were male. The average age of the subjects in the study was 18.06 years old with a minimum age of 14 years and maximum 27 years (Table 1).

Variables	No. of patient (%)
<b>Sex</b>	
Female	32 (62,7)
Male	19 (37,3)
<b>Phototype</b>	
Phototype II	6 (11,7)
Phototype III	27 (52,9)
Phototype IV	18 (35,2)
<b>Clinical classification</b>	
Mild	51 (100)
<b>Age</b>	
Average	18.06 years
Std. Deviation	3.331 years

Minimum	14 years
Maximum	27years

**Table 1:** Patients demographic data treated with phototherapy.

## The Inclusion Criteria Applied for Phototherapy

Age over 14 years old, general good health, the ability of complying with the study protocol and an acne severity grade of mild to moderate form.

## Exclusion criteria hormonal/endocrinal disorders

Exclusion criteria hormonal/endocrinal disorders, pregnant or lactating, having a history with herpes simplex, suffer of collagenases, have been treated with retinoid within the past 6 months, treated with sulphonamides, tetracycline, thiazides, antidepressant tricyclic, anti-inflammatory non-steroidal, suffer from epilepsy, have a history of skin cancer, have tanned by sun within the last 30 days.

## Treatment's Parameters of Phototherapy

Before the treatment, depending on the skin's phototype, the energy level setting was done by which of the patients would be treated (Table 2).

	Phototype II	Phototype III	Phototype IV
Session I	50	40	30
Session II	60	50	40
Session III	70	60	50
Session IV, V, VI, VII, VIII	80	70	60

**Table 2:** Energy level setting by skin phototype.

The full treatment of patients was conducted in eight sessions. Treatments were administered twice a week for a four week period. Each session consisted of two consecutive applications that last 10-15 min. In the second application the energy level was raised by 5-10 units. Adjustable pulse durations 35 ms and an optical fluence of 3.5 J/cm<sup>2</sup> per pulse.

Pulses per face treatment was about 40, the device used for treatment was skin station, production of Radiancy Company. The device emits light energy with wavelengths 430-1100 nm.

## Clinic Evaluation Parameters

**The main clinical indicators studied where the non-inflammatory elements were included**

Closed comedones (white) and open come done (blackhead) and inflammatory elements including: papules and pustules. These indicators for patients treated with Phototherapy, were assessed at the end of the second, fourth, sixth, eighth sessions, one month after treatment and after 2, 4, 6, 8, 10, 12 weeks for the patients treated with standard treatment, where patients were photographed by a Sony 12 megapixel digital camera.

### Results of Clinical Parameters

One month after the treatment with Phototherapy, the inflammatory and non-inflammatory elements cleaning, reached  $67.9 \pm 6.2\%$  in mild form and  $68.4 \pm 6.5\%$  in moderate form of Acne vulgaris. After 8 sessions of treatment with phototherapy, inflammatory elements show greater improvements as compared to non-inflammatory ones ( $p=0.001$ ). The results of the one month long treatment (eight sessions) are converted in percentage as follows:

Percentage presentation of the decrease of inflammatory, non-inflammatory and total elements before treatments, after 2 sessions, four sessions, six sessions, eight sessions and one month after treatment.

All patients completed the treatment according to the treatment protocols of photo therapy (LHE), with minimum side effects. A positive response was seen in all patients during treatment with photo therapy (LHE). By continuously monitoring the patients, it was found that the effect of treatment was almost undetectable after the first two sessions, and became noticeable after four sessions. The effect increased further as the treatment progressed. At the end of the treatment (after eight sessions), it was seen that important statistical differences existed between inflammatory and non-inflammatory elements as compared to the pre-treatment average baseline.

	Mild grade
	Average $\pm$ SD
The difference in the number of elements (total) between the start and end of therapy	19 4.4
The percentage of improvement of clinical signs	67.9 6.2
the difference in the number of inflammatory elements (start and end of therapy)	10.8 2.1
the percentage of improvement of clinical signs inflammatory elements	70.4 6.9

Photo type	Average + Standard Deviation	Average + Standard Deviation (%)
2	$71.2 \pm 5.8$	$68.2 \pm 4.9$
3	$68.6 \pm 6.5$	$67.7 \pm 7.2$
4	$66.8 \pm 6.1$	$67 \pm 6.3$

**Table 5:** The percentage of improvement of clinical signs by photo type skin with acne vulgaris in patients treated with phototherapy.

In Table 5, no changes in total treatment effect according to photo type in the case of acne vulgaris mild.

Compare the photo type setting no significant change in percentage of improving the clinical signs of acne vulgaris in patients with mild form. Photo type is not to assess the effectiveness of treatment with phototherapy acne vulgaris. One month after the treatment stated in percentage, this effect was  $70.4 \pm 6.9\%$  inflammatory elements and  $63.3 \pm 12.4\%$  for non-inflammatory elements in mild form (Figures 1 to 4).

the difference in the number of non-inflammatory elements (start and end of therapy)	8.07 3.4
The percentage of improvement of clinical signs non-inflammatory elements	63.3 12.4

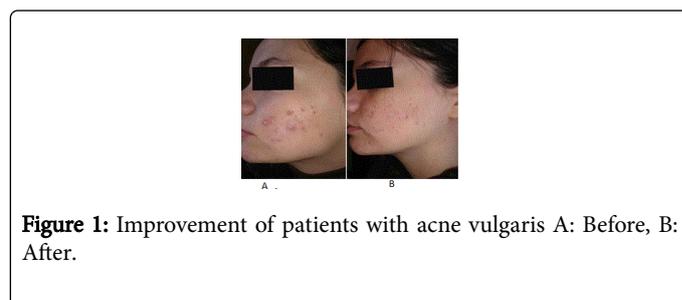
**Table 3:** Comparison of phototherapy on acne vulgaris.

Table 3, appear averages and standard deviation in the difference in the occurrence of clinical signs of acne vulgaris before and after treatment and% of improving the clinical signs (total elements, inflammatory and non-inflammatory elements). When analyzed in percentage, the improvement is better significantly in inflammatory elements while percentage improvement in total elements and elements non-inflammatory don't have significant changes.

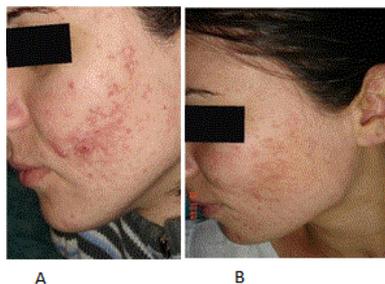
Gendered	Grade	Average + standard deviation (%)
Male	Mild	$68.2 \pm 4.9$
Female	Mild	$67.7 \pm 7.2$
Total	Mild	$67 \pm 6.3$

**Table 4:** Overall the percentage of improvement of clinical signs by gender of acne vulgaris treatment with phototherapy.

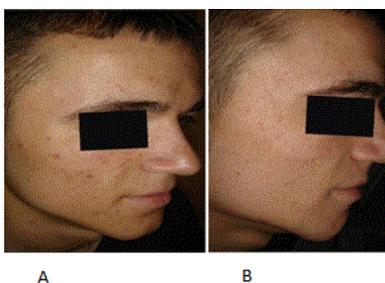
In Table 4, the improvement of clinical signs presented in % reduction in the number of inflammatory and non-inflammatory elements is under treatment and gender. When analysing the t test is not made in response to significant changes in the two ranks phototherapy of acne vulgaris by gender. No changes in total treatment effect according to sex in the case of acne vulgaris mild and moderate grade.



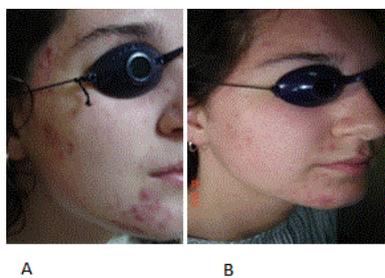
**Figure 1:** Improvement of patients with acne vulgaris A: Before, B: After.



**Figure 2:** Improvement of patients with acne vulgaris A: Before, B: After.



**Figure 3:** Improvement of patients with acne vulgaris, A: Before, B: After.



**Figure 4:** Improvement of patients with acne vulgaris, A: Before, B: After.

In the second group study included the total of 47 patients with mild form of acne vulgaris they were treated locally with Adapalene 0.1% Gel. The average age of the subjects in the study was 18.7 years old with a minimum age of 13 years and maximum 27 years.

### Exclusion Criteria

Exclusion criteria prohibited enrolment of subjects with acne requiring isotretinoin therapy or other dermatologic conditions requiring interfering treatment. Women were excluded if they were under hormonal/endocrinal disorders, pregnant, nursing or planning a pregnancy as were men with facial hair that would interfere with the assessments (Table 6).

Variables	No. of patient standard treatment (%)
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Sex	
Female	26 (55.3)
Male	21 (44.7)
Clinical classification	
Mild	47 (100)
Age	
Average	18.7 years
Std. Deviation	3.587 years
Minimum	13 years
Maximum	27 years

**Table 6:** Patients demographic data treated with standard treatment.

### Results

The results of 12 weeks treatment are converted in percentage as follows

Percentage presentation of the decrease of inflammatory, non-inflammatory and total elements before treatments, after 2 weeks, 4 weeks, 6 weeks, 8 weeks, 10 weeks and 12 weeks. At the end of the treatment (after eight sessions) it was seen that important statistical differences existed between inflammatory and non-inflammatory elements as compared to the pre-treatment average baseline. After three months treatment with local treatment, the inflammatory and non-inflammatory elements cleaning, reached  $59.4 \pm 5.8\%$  (Table 7 and Figures 5 and 6).

	Mild grade Average $\pm$ SD
The difference in the number of elements (total) between the start and end of therapy	15.9 $\pm$ 2.8
The percentage of improvement of clinical signs	59.4 $\pm$ 5.8
the difference in the number of inflammatory elements (start and end of therapy)	8.1 $\pm$ 2.4
the percentage of improvement of clinical signs inflammatory elements	59.3 $\pm$ 9.7
the difference in the number of non-inflammatory elements (start and end of therapy)	7.7 $\pm$ 1.2
The percentage of improvement of clinical signs no inflammatory elements	58.9 $\pm$ 6.8

**Table 7:** Comparison of local treatment on acne vulgaris.

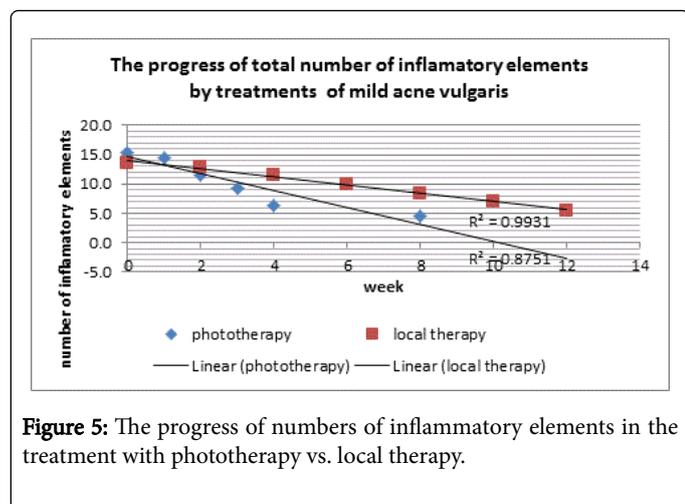


Figure 5: The progress of numbers of inflammatory elements in the treatment with phototherapy vs. local therapy.

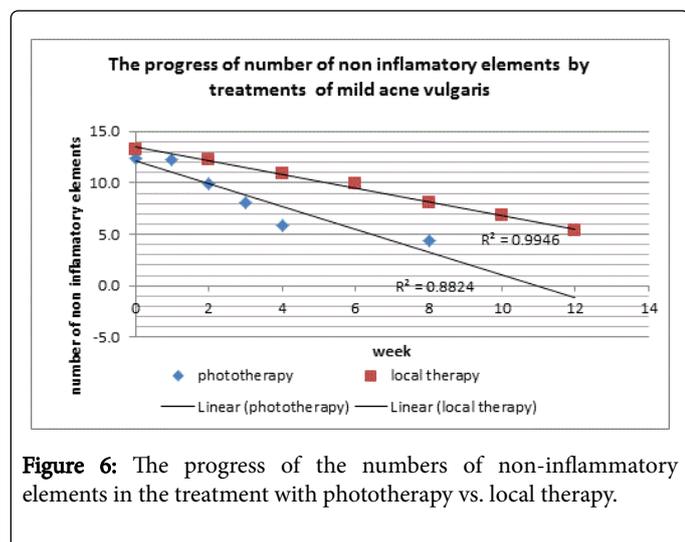


Figure 6: The progress of the numbers of non-inflammatory elements in the treatment with phototherapy vs. local therapy.

## Discussion

The results show that phototherapy, pulsating light heat energy (LHE) emitted by the Skin Station apparatus, is an effective and rapid treatment compared to any other alternative treatment. The continuous monitoring of the patients before, during and one month after the treatment showed satisfactory results in clearing out the inflammatory and non-inflammatory elements of acne vulgaris (Figure 7 and Table 8).

Week	Local Therapy	Phototherapy
0	26.85	27.88
1		26.53
2	25.25	21.39
3		17.35
4	22.4	12.29
5		
6	19.58	

8	16.52	8.88
10	13.85	
12	10.92	

Table 8: The progress of the total numbers of elements in the treatment with phototherapy vs. local therapy.

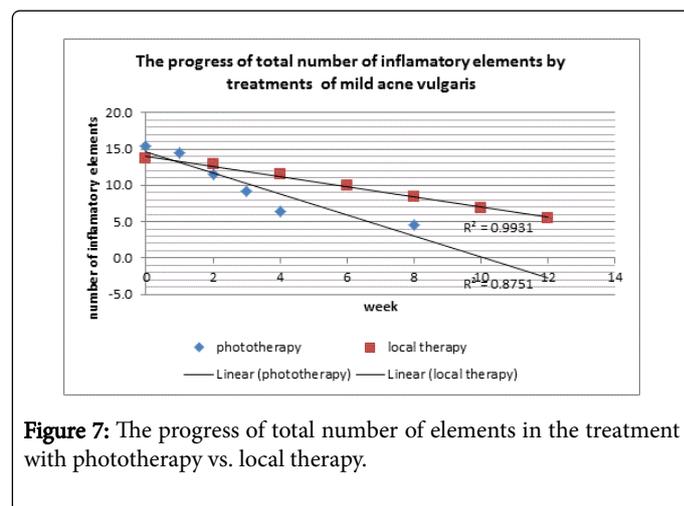


Figure 7: The progress of total number of elements in the treatment with phototherapy vs. local therapy.

Phototherapy appears to be effective and with satisfactory results in clearing out the inflammatory and non-inflammatory elements at the end of the treatment, as well as one month after the treatment. The results are better for the inflammatory elements. The results are statistically equal for both genders, independent of age. The results are statistically equal for both the photo types II, III, IV. Phototherapy LHE has obliterating and anti-inflammatory effects P acnes. Propionibacterium acnes are an obvious target for acne phototherapy since it is central to the inflammatory process<sup>11</sup>. P.acnes makes porphyrins, which are present in the follicle, in proportion to its population. Once the porphyrin is exposed to visible light, it becomes chemically active and transfers to an excited state, resulting in the formation of singlet oxygen, which combines with cell membranes to destroy the *P. acnes* [1,2,10]. This process is depended on the rate of production of excited porphyrin molecules, which is influenced by the concentration of porphyrin, the concentration of photons, the temperature and the wavelength of photons [8]. Phototherapy has an obvious advantage in the treatment of mild grade of Acne vulgaris compared with local treatment

## Conclusion

Although topical and oral therapies are considered the first line of treatment, significant adverse side effects or bacterial resistance may exist. Thus, there is an unmet need for well-tolerated therapy that provides effective acne clearance without the risk of side effects.

Recently, a significant advancement in photobiology and laser/light-based technology created new possibilities to treat acne. Based on successful *in vitro* and *in vivo* studies and human clinical trials conducted in the last 5 years, it is evident that the amelioration of acne with light-based therapy is comparable to the effects of oral antibiotics, and improvement is maintained for several months. Furthermore, it appears that these systems offer faster resolution and fewer side effects and lead to patient satisfaction. Based on this study it is concluded that

phototherapy applied with LHE technology is effective treatment option for patients who cannot or chose not to take medications.

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