

## The effectiveness of phototherapy compared to standard medication in the treatment of Acne Vulgaris

**Artur Bani<sup>1</sup>, Niko Pecani<sup>2</sup>, Ermira Vasili<sup>2</sup>, Mevlud Hoxha<sup>1</sup>,  
Anisa Kondakciu<sup>3</sup>, Sonila Xinxo<sup>4</sup>**

<sup>1</sup>Regional Hospital, Berat, Albania;

<sup>2</sup>University Hospital Center "Mother Teresa", Tirana, Albania;

<sup>3</sup>Health Center, Kutalli, Berat, Albania;

<sup>4</sup>Institute of Public Health, Tirana, Albania.

**Corresponding author:** Artur Bani, MD;  
Address: Regional Hospital, Berat, Albania;  
E-mail: arturbani@yahoo.com

### Abstract

**Aim:** To assess the effectiveness of phototherapy with Pulsed Light and Heat Energy (LHE) versus local and local and systemic medication in the treatment of mild and moderate forms of acne.

**Methods:** This study involved 235 individuals with various forms of Acne vulgaris in Berat region, Albania. During a period of five years, there were treated with phototherapy 119 patients with Acne vulgaris (68 with a moderate form and 51 with a mild form), whereas 116 patients underwent standard treatment (48 patients with a mild form and 68 patients with a moderate form). Assessment of treatment effectiveness was based on the number of inflammatory and non-inflammatory elements at the beginning of the therapy and in the intervals after 2 sessions, 4 sessions, 6 sessions, 8 sessions, 1 month after treatment with Phototherapy and 2, 4, 6, 8, 10, and 12 weeks after standard treatment.

**Results:** One month after the treatment with Phototherapy, the inflammatory and non inflammatory elements cleaning reached  $67.9 \pm 6.2\%$  in the mild form and  $68.4 \pm 6.5\%$  in the 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 the mild form and  $71.4 \pm 7.2$  after treatment with local plus systemic in the 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:** acne vulgaris, phototherapy, standard treatment.

## Introduction

Acne vulgaris is a frequent skin disease affecting 80%-85% of adolescents and young adults at any time during their lives. Acne vulgaris is the most common skin disease and is characterized by non-inflammatory, open or closed comedones and by inflammatory papules, pustules, 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, hyperproliferation of *Propionibacterium acnes*, and an inflammatory response initiated by bacterial antigens and cytokines (1).

*P. acnes* is 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).

Studies have shown that *P. acnes* activates the toll-like (TL) receptor 2 on monocytes and neutrophils. Activation of the TL receptor 2 then leads to the production of multiple proinflammatory cytokines, including interleukins (IL) 12 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 (3,4). Inflammation may be a primary phenomenon or a secondary phenomenon.

To date, the evidence suggests a secondary inflammatory response to *P. acnes* (4,5). However, IL-alpha expression has been identified in micro-comedones, and it may play a role in the develop-

ment of acne (6,7).

*Propionibacterium acnes* is 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 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* (8).

This process depends 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).

The aim of this study was to compare the clinical efficacy of Phototherapy (LHE) compared to the standard treatment of acne vulgaris in Albanian patients.

## Methods

This study involved 235 individuals with various forms of acne vulgaris in Berat region, Albania. During a period of five years, there were treated with phototherapy 119 patients with Acne vulgaris (68 with a moderate form and 51 with a mild form), whereas 116 patients underwent standard treatment (48 patients with a mild form and 68 patients with a moderate form).

In the first group, the study included a total of 119 patients treated with phototherapy with a mean age of  $18.1 \pm 3.3$  years (62.5% were females and 37.5% were males). The minimum age was 14 years and the maximum was 27 years (Table 1).

**Table 1. Demographic data of the patients treated with phototherapy**

Variable	N (%)
<b>Sex</b>	
Female	76 (62.5)
Male	43 (37.5)
<b>Phototype</b>	
Phototype II	11 (9.2)
Phototype III	66 (55.5)
Phototype IV	42 (35.3)
<b>Clinical classification</b>	
Mild	51 (42.9)
Moderate	68 (57.1)
<b>Age (years)</b>	
Average	18.1
Standard deviation	3.3
Minimum	14
Maximum	27

The inclusion criteria applied for Phototherapy included: age over 14 years old, general good health, the ability to comply with the study protocol and an acne severity grade of mild to moderate form. Exclusion criteria included patients under 13 years old, pregnant or lactating women, having a history with herpes simplex, suffering from collagenosis, having been treated with retinoid within the past six months, treated with sulfonamides, tetracycline,

thiazides, antidepressant tricyclic, non-steroidal anti-inflammatory drugs, suffering from epilepsy, history of skin cancer, or sun burn within the last 30 days.

#### ***Treatment parameters of phototherapy***

Depending on the skin's phototype, the energy level setting was done for each patient before commencing the treatment (Table 2).

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

	Phototype II	Phototype III	Phototype IV
<b>Session I</b>	50	40	30
<b>Session II</b>	60	50	35
<b>Session III</b>	70	60	40
<b>Session IV</b>	80	70	50

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 10-15 minutes long. In the second application, the energy level was raised by 5-10 units. The device used for the treatment was SkinStation, production of Radiancy Company. This device emits light energy with wavelengths 430-1100 nm, with energy intensity 3.5 J/cm<sup>2</sup>, and with pulse durations of 35 ms.

The second group included 116 patients treated with

phototherapy with a mean age of 18.7 ± 3.6 years (52.6% were females and 47.4% were males). There were 47 patients with a mild form of acne vulgaris treated locally with Adapalene 0.1% + Clindamicin 1%, while 68 patients with a moderate grade were treated with Adapalene 0.1% + Clindamicin 1% + Doxacycline 100 mg daily for 12 weeks. The average age of the subjects in this group was 18.7 years with a minimum age of 13 years and a maximum 27 years. Exclusion criteria prohibited enrollment of subjects with acne requiring

isotretinoin therapy or other dermatologic conditions requiring interfering treatment. Women were excluded if they were pregnant, in lactation, or

planning a pregnancy, as were men with facial hair that would interfere with the assessments.

**Table 3. Demographic data of the patients under standard treatment**

Variables	N (%)
<b>Sex</b>	
Female	61 (52.6)
Male	55 (47.4)
<b>Clinical classification</b>	
Mild	48 (41.4)
Moderate	68 (58.6)
<b>Age (years)</b>	
Average	18.7
Standard deviation	3.6
Minimum	13
Maximum	27

### *Evaluation of the clinical parameters*

The main clinical indicators included: closed comedones (white) and open comedone (black-head) 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 the treatment and after 2, 4, 6, 8, 10, and 12 weeks for the patients treated with standard therapy (all patients were photographed with a Sony 12 megapixel digital camera).

### *Statistical analysis*

The numerical variables were summarized by their mean values and standard deviations, whereas the categorical variables were presented in absolute values and their respective percentages.

Numerical 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 analyzing the differences between the categorical variables. A p-value of  $\leq 0.05$  was considered as statistically significant in all cases.

### **Results**

One month after the treatment with Phototherapy, the inflammatory and non inflammatory elements cleaning reached  $67.9\% \pm 6.2\%$  in the mild form and  $68.4\% \pm 6.5\%$  in the moderate form of Acne vulgaris.

After eight sessions of treatment with phototherapy, inflammatory elements showed greater improvements as compared to the non-inflammatory ones ( $P=0.001$ ).

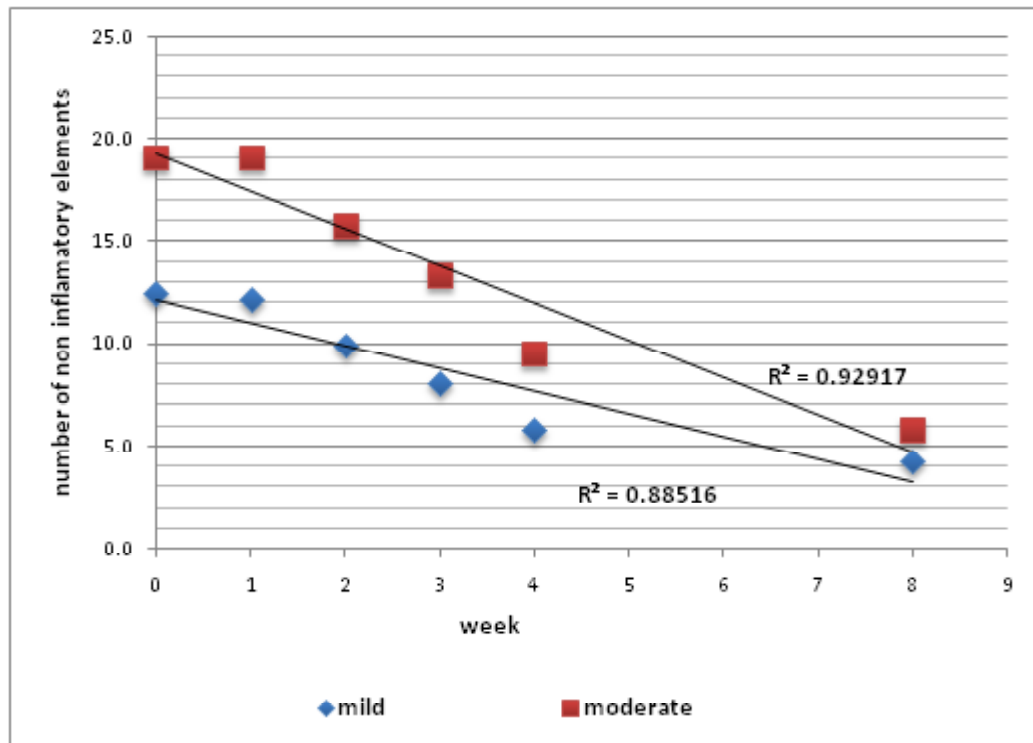
The results of the one-month treatment (eight sessions) are converted in percentages as follows: percentage presentation of the decrease of inflammatory, non-inflammatory and total elements before treatments, after two sessions, four sessions, six sessions, eight sessions and one month after treatment.

All patients completed the treatment according to the treatment protocols of phototherapy (LHE), with minimum side effects. A positive response was observed in all patients during treatment with phototherapy (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 (Figure 1). At the end of the treatment (after eight sessions), important statistical

differences were noted between the inflammatory and non-inflammatory elements as compared to the pre-treatment average baseline values (Table 4).

**Figure 1. The progress in the number of non-inflammatory elements in the treatment with phototherapy according to the degree of disease**



**Table 4. Performance of the total number of non-inflammatory elements (average) in the treatment with phototherapy according to the degree of disease**

Week	Mild grade	Moderate grade
0	12.4	19.2
1	12.2	19.1
2	9.9	15.8
3	8.1	13.3
4	5.9	9.6
8	4.3	5.8

When analyzed in percentages, the improvement was statistically significant in inflammatory elements, whereas the percentage improvements

in the total elements and non-inflammatory elements were not statistically significant (Table 5).

**Table 5. Comparison of phototherapy on acne vulgaris according to the disease grade**

	<b>Mild grade</b> Average $\pm$ SD	<b>Moderate grade</b> Average $\pm$ SD	<b>P-value</b>
The difference in the number of elements (total) between the start and the end of therapy	19 $\pm$ 4.4	30.3 $\pm$ 5.7	0.001
The percentage of improvement of clinical signs	67.9 $\pm$ 6.2	68.4 $\pm$ 6.5	0.694
The difference in the number of inflammatory elements (start and end of therapy)	10.8 $\pm$ 2.1	18.1 $\pm$ 3.2	0.001
The percentage of improvement of clinical signs inflammatory elements	70.4 $\pm$ 6.9	71.4 $\pm$ 7.2	0.001
The difference in the number of non-inflammatory elements (start and end of therapy)	8.07 $\pm$ 3.4	12.2 $\pm$ 2.8	0.447
The percentage of improvement of clinical signs of non-inflammatory elements	63.3 $\pm$ 12.4	64.2 $\pm$ 8.2	0.614

There were no changes in the effect of total disease (mild vs. moderate form of acne vulgaris) treatment according to gender and degree of the [Table 6].

**Table 6. Percentage of improvement of clinical signs by gender and degree of Acne vulgaris treated with phototherapy**

<b>Gender</b>	<b>Grade</b>	<b>Average and standard deviation (%)</b>
<b>Male</b>	Mild	68.2 $\pm$ 4.9
	Moderate	68.4 $\pm$ 7.5
	Total	68.3 $\pm$ 6.3
<b>Female</b>	Mild	67.7 $\pm$ 7.2
	Moderate	68.4 $\pm$ 6.1
	Total	68.1 $\pm$ 6.5
<b>Total</b>	Mild	67 $\pm$ 6.3
	Moderate	68.4 $\pm$ 6.5
	Total	68.2 $\pm$ 6.4

In the second group, three months after the treatment with local treatment, the inflammatory and non-inflammatory elements cleaning reached 59.4 $\pm$ 5.8 in the mild form and 71.4 $\pm$ 7.2 in the moderate form of Acne vulgaris.

The results of 12 weeks treatment are converted

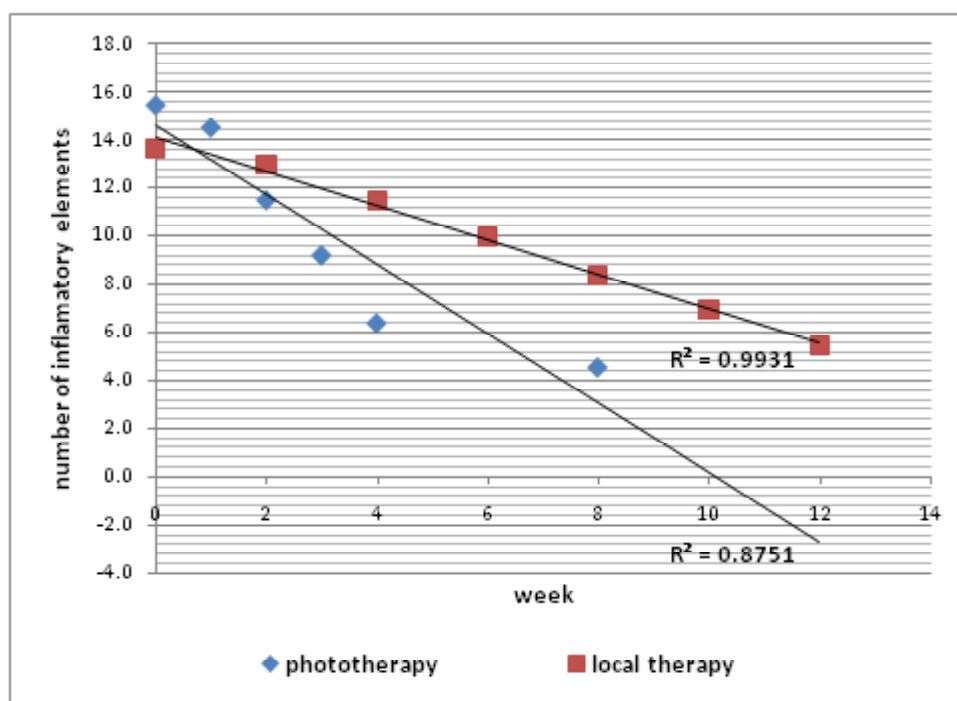
in percentage as follows: percentage presentation of the decrease of inflammatory, non-inflammatory and total elements before treatments, after 2 weeks, 4 weeks, 6 weeks, 8 weeks, 10 weeks and 12 weeks after treatment.

At the end of the treatment (after eight sessions),

it was noted an important statistical difference between the inflammatory and the non-inflammatory

elements as compared to the pre-treatment average baseline values (Figure 2).

**Figure 2. The progress in the number of inflammatory elements in the treatment with phototherapy vs. local therapy**



Compared with the phototype setting, no significant changes in the percentage of improving the clinical signs of acne vulgaris in patients with mild or moderate forms was noted.

One month after the treatment, this effect was  $70.4\% \pm 6.9\%$  for the inflammatory elements and  $63.3\% \pm 12.4\%$  for the non-inflammatory elements in the mild form, whereas it was  $71.4\% \pm 7.2\%$  for the inflammatory elements and  $64.2\% \pm 8.2\%$  for the non-inflammatory elements in the moderate form.

One month after the treatment, the inflammatory and non-inflammatory elements cleaning reached  $67.9\% \pm 6.2\%$  in the mild form and  $68.4\% \pm 6.5\%$  in the moderate form of Acne vulgaris.

T-test results indicated that the percentage of improvement in all clinical signs was the highest in the phototherapy treatment group. Hence, it was

a faster improvement which was more visible in the treatment of Acne vulgaris with phototherapy. Regarding the of treatment with phototherapy compared with local plus systemic treatment results, the percentage of improvement of clinical signs associated with inflammatory elements and the total was higher, whereas the percentage of improvement in non-inflammatory elements had no significant changes. Thus, the effect of local plus systemic treatment indicated a positive effect in the treatment of inflammatory Acne vulgaris elements. The effectiveness of phototherapy in the elimination of inflammatory and non-inflammatory elements was very visible compared with the local treatment, while the effectiveness of elimination of inflammatory and non-inflammatory elements was somehow lower for the local plus systemic treatment compared with the phototherapy alone.

## Discussion

The results of this study showed 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.

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 more positive for the inflammatory elements.

The findings from the current study were statistically significant in for both genders, independent of age. Also, findings were statistically significant for both the mild and the moderate forms of the disease. In addition, the results were somehow similar for both the phototypes II, III, and IV. Phototherapy LHE has obliterating and anti-inflammatory effects on the Propionibacterium (*P. acnes*). *P. acnes* is an obvious target for acne phototherapy since it is central to the inflammatory process (9,10).

*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 depends 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 (8).

Phototherapy has an obvious advantage in the treatment of mild grade of Acne vulgaris compared with the local treatment and a slight disadvantage in the treatment of moderate grade of Acne Vulgaris compared with the local plus systemic treatment.

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 has created new possibilities to treat acne. Based on successful in vitro and in vivo studies and human clinical trials conducted in the last five 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 a faster resolution and fewer side effects and lead to a higher patient satisfaction.

Based on the current study, it is concluded that phototherapy applied with LHE technology is an effective treatment option for patients who cannot take medications.

**Conflicts of interest:** None declared.

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