

## Efficacy of Low-Level Laser Versus Topical Erythromycin 2% in the Treatment of Inflammatory Acne Vulgaris

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**ABSTRACT** **Introduction:** Acne vulgaris is a skin problem affecting many people of different ages. Despite many options that are available for treatment of acne vulgaris, many patients still respond inadequately to treatment. Phototherapy is one of the best acne treatment options.

**Objectives:** It was to compare the efficacy of low-level laser therapy in treatment of inflammatory acne versus topical erythromycin 2% cream.

**Methods:** This study included 40 patients (18 males, 22 females) with different clinical severities of acne vulgaris. All the participants underwent split-face treatment: one side with 8 treatments (twice per week) of a low-level continuous infrared diode laser (808 nm) wavelength and (500 Hz) frequency and the other side with topical erythromycin 2% twice daily (aknemycin cream 2%). Evaluation was done at start of sessions, 2 weeks after the end of sessions and 3 months after stoppage of treatment depending on: photographs, global evaluation of acne scale, and Indian acne association grading.

**Results:** There was improvement of acne lesions on laser side and antibiotic side (assessed as non-inflammatory and inflammatory lesion counts). Laser side showed better results than antibiotic side. Patients were more satisfied with laser treatment due to minimal side effects and less relapse.

**Conclusions:** A series of 8 treatments using low level continuous infrared diode laser represents a cheap, safe and effective non-invasive therapeutic option for acne vulgaris.

## Introduction

Acne vulgaris (AV) is a common disease of the pilosebaceous unit (PSU) of the skin and may be either non-inflammatory (open and closed comedones) or inflammatory (papules and pustules) [1]. Traditional treatments for AV include topical medications such as antibiotics, retinoids, benzoyl peroxide (BPO), alpha hydroxyl acids (AHA), salicylic acid (SA), or azelaic acid (AA). In severe cases, systemic antibiotics such as tetracycline and doxycycline, oral retinoids, and some hormones are indicated. Despite many options available for treatment of AV, many patients still respond inadequately to treatment [2]. Phototherapy (light, lasers and photodynamic therapy (PDT)) has been proposed as an alternative therapeutic modality to treat AV with fewer side effects compared to other treatment options [3]. Low-level laser therapy (LLLT) is a fast-growing technology used to treat conditions that require stimulation of healing, relief of pain and inflammation, and restoration of function [4]. This approach has also been used for inflammatory acne by decreasing expression of cyclooxygenase 2 (cox-2) enzyme leading to inhibition of production of pro-inflammatory cytokines like tumor necrosis-alpha (TNF- $\alpha$ ) and interleukin 1alpha (IL-1 $\alpha$ ) and so reduce inflammation [5,6]. The LLLT involves exposing cells to low levels of red and near infrared (NIR) light which is called 'low-level' because the energy or power densities employed are low compared to other forms of laser [7].

## Objectives

It was to compare the efficacy of low-level laser therapy in treatment of inflammatory acne versus topical erythromycin 2% cream.

## Methods

This study was right-left comparative study on 40 patients with inflammatory AV. They were selected from the Outpatient Clinic of Dermatology and Venereology Department, Faculty of Medicine, Tanta University Hospitals.

## Inclusion Criteria

1. Patients suffering from inflammatory AV.
2. Patients who did not receive systemic or topical treatment 6 weeks before enrollment in the study.

## Exclusion Criteria

Pregnancy, breast feeding, subjects with dermatological diseases other than acne, chronic diseases such as chronic liver and renal diseases, autoimmune diseases, photosensitive patients and patients using photo-sensitive drugs, cancer, pacemaker, epileptic seizures.

## Study Assesemnets

All patients were subjected to history taking, examination, evaluation by:

1. The GEA (Global Acne Severity) Scale: based on photographic and clinical assessment of acne patients (Table 1). This assessment was done before starting therapy, at the end of 8 sessions of the therapy (after 1 month) and 3 months after stoppage of any treatment.
2. The Indian Acne Association (IAA) grading: based on type and number of acne lesions (Table 2).

Every patient received an explanation of nature, risks and purpose of the study, an informed consent was obtained, digital photographs were taken before starting therapy and at every visit till the end of the therapy and 3 months after that.

## Therapeutic Regimen

1. In this study 40 patients with inflammatory acne were subjected to be treated by LLL (ENDOLASER 422. Enraf-nonius B. V, Netherlands). It is a low level continuous IR diode laser (808nm) wave length and (500HZ) frequency with a peak power of 500mW. The laser probe is 500 Mw continuous laser diode (LP500) with peak power of 500 W.

**Table 1. Global evaluation of acne scale.**

0	Clear, no lesions	Residual pigmentation and erythema may be seen
I	Almost clear, almost no lesions	A few scattered open or closed comedones and very few papules
II	Mild	Easily recognizable: Less than half of the face is involved. A few open or closed comedones and a few papules and pustules
III	Moderate	More than half of the face is involved. Many papules and pustules or many open or closed comedones. One nodule may be present
IV	Severe	Entire face is involved, covered with many papules and pustules, open or closed comedones and rare nodules
V	Very severe	Highly inflammatory acne covering the face with presence of nodules

**Table 2. Indian acne association grading of acne severity.**

Grades	Comedones	Papules/Pustules	Nodules
Mild	<30	<10	None
Moderate	Any number	>10	<3
Severe	Any number	Any number	>3

- The patients were treated as split face (one side treated with topical erythromycin 2% twice daily and the other side with LLL device) in Physical Medicine Department, Faculty of Medicine, Tanta University Educational Hospital.
- Number of sessions was 2 per week for 4 weeks.
- Methods of application of cold laser: Patient was seated in a comfort position and wore protective glasses (Endolaser 422). The probe was in contact with the treated area by multiple applications of cold laser in multiple points. The probe was applied for 5 minutes per point of the affected area with the dose of 1.5 J/cm<sup>2</sup>.
- The patients were advised not to use any other treatment for acne during laser therapy and 3 months after last session.
- Side effects were reported by the patients.

#### Assessment of the Efficacy of the Therapeutic Procedure

- Photographs: They were taken at baseline and before each session then after 3 months of last session for follow up. Photos were taken by Samsung ST150F smart compact camera, 5x telephoto, F2.5 lens, and 16.2 MP resolution.
- The GEA scale: of the inflammatory acne lesions before starting treatment, 2 weeks after the last session and three months later.
- The IAA grading: according to number and type of the lesions.
- Three blinded dermatologists: were asked to record percentage of improvement for each patient after completion of the treatment by comparing digital photographs before starting treatment and 2 weeks after the last session according to quartile grading scale: No improvement: if improvement was 0%, fair improvement: 0-25%, moderate improvement: 26-50%, marked improvement: 51-75%, excellent improvement: 76-100%.
- Patient satisfaction: whether the patient was unsatisfied, slightly satisfied, satisfied or very satisfied.

#### Follow-up

Follow up of the patients after end of treatment sessions monthly for 3 months to observe efficacy, recurrence or side effects.

#### Statistical Analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (IBM Corp) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level. The used tests were Chi-square test, McNemar and marginal homogeneity test, Wilcoxon signed ranks test, Kruskal Wallis test and F-test (ANOVA).

P value was considered statistically significant at  $P \leq 0.05$ , and statistically high significant at  $P < 0.001$ .

#### Results

Clinical results were demonstrated in Table 3. Comparison between laser and antibiotic side (Table 4). Comparison between two sides according to type of lesions (Table 5). Degree of improvement (Table 6). There was no statistically significant difference between both sides except in relapse where

**Table 3. Demographic data of the studied cases (N = 40).**

Parameter		N	%
Gender	Male	18	45.0
	Female	22	55.0
Age	Range	17.0-22.0	
	Mean ± SD	19.25 ± 1.65	
	Median (IQR)	19.0 (18.0 – 21.0)	
Duration (years)	Min. – Max	0.50 – 7.0	
	Mean ± SD.	3.53 ± 1.77	
	Median (IQR)	3.50 (2.0 – 5.0)	
	Family history		
No	22	55.0	
Yes	18	45.0	
Aggravating factors	No	6	15.0
	Sun exposure	2	5.0
	Sun exposure, food	4	10.0
	Food	10	25.0
	Menses	10	25.0
	Sun exposure, menses	6	15.0
	Sun exposure, menses, food	2	5.0
Laser side	Right	12	30.0
	Left	28	70.0
Type of lesion	Papulopustular	30	75.0
	Nodulocystic	10	25.0

IQR = Inter quartile range; SD = Standard deviation.

**Table 4.** Comparison between laser and antibiotic side according to result of treatment.

Result	Laser side (n = 40)		Antibiotic side (n = 40)		Test	P
	No.	%	No.	%		
GEA					$\chi^2 = 3.584$	0.025
I	34	85.0	24	60.0		
II	6	15.0	16	40.0		
III	0.0	0.0	0.0	0.0		
IV	0.0	0.0	0.0	0.0		
V	0.0	0.0	0.0	0.0		
IAA grading					MH= 6.0	1.000
No	24	60.0	22	55.0		
Mild	16	40.0	16	40.0		
Moderate	0	5.0	1	5.0		
Severe	0	0	0	0		

McN = McNemar test; MH = Marginal Homogeneity Test:

**Table 5.** Comparison between number of different types of lesions before and after treatment.

Number of lesion	Laser side		Antibiotic side		P <sup>a</sup>	P <sup>b</sup>
	Before	After	Before	After		
<b>Papules</b>	<b>40(100%)</b>	<b>7(35%)</b>	<b>40(100%)</b>	<b>18(45%)</b>		
Min. – Max.	2.0 – 35.0	0.0 – 25.0	2.0 – 38.0	0.0 – 8.0	0.541	0.721
Mean ± SD.	11.55 ± 9.75	2.50 ± 5.74	11.65 ± 10.37	2.30 ± 2.94		
Median (IQR)	8.50 (4.5-15.5)	0.0 (0.0-2.50)	6.50 (5.0-13.50)	0.0 (0.0-5.50)		
P	<0.001		<0.001			
<b>Nodules</b>	<b>5(25%)</b>	<b>1(5%)</b>	<b>6(30%)</b>	<b>0(0%)</b>		
Min. – Max.	0.0 – 3.0	0.0 – 1.0	0.0 – 2.0	0.0 – 0.0	0.317	0.317
Mean ± SD.	0.60 ± 1.10	0.05 ± 0.22	0.45 ± 0.76	0.0 ± 0.0		
Median (IQR)	0.0(0.0 – 1.0)	0.0(0.0-0.0)	0.0 (0.0 – 1.0)	0.0		
P	0.041		0.024			
<b>Comedones</b>	<b>11(55%)</b>	<b>6(30%)</b>	<b>18(45%)</b>	<b>4(20%)</b>		
Min. – Max.	0.0 – 25.0	0.0 – 23.0	0.0 – 25.0	0.0 – 22.0	0.503	0.725
Mean ± SD.	7.0 ± 9.29	3.25 ± 6.20	5.80 ± 8.19	2.60 ± 5.95		
Median (IQR)	3.0(0.0 – 14.0)	0.0(0.0-5.0)	0.0 (0.0 -10.0)	0.0(0.0-0.0)		
P	0.040		0.043			

IQR = Inter quartile range; SD = Standard deviation.

<sup>a</sup>P value for Wilcoxon signed ranks test for comparing between laser side and antibiotic side before treatment

<sup>b</sup>P value for Wilcoxon signed ranks test for comparing between laser side and antibiotic side after treatment

laser side showed less relapse than antibiotic side (Table 7). Evaluation of follow up after 3months of both modalities of treatment according to the GEA scale (Table 7). Figures 1-3 show the change occurs from the start of the treatment to three months after the treatment and also comparing the antibiotic and laser sides in three cases.

## Conclusions

In the current study, there was improvement in acne after treatment according to the GEA scale. By comparing both

sides, laser side was better in treatment of AV than antibiotic side.

Our results were supported by study of Szymańska et al as they showed that treatment of acne with a LLLT for 10 minutes by a device with a power of 360 mW emits IR radiation with a wavelength of 785 nm and a power density of 80 mW/cm<sup>2</sup> showed significant improvement in acne lesions and decrease in skin sebum excretion was observed after the treatment with no adverse effects [9].

Other studies proposed that blue and red light may act synergistically in improving acne by combining anti-bacterial

and anti-inflammatory action, rendering phototherapy with blue (415 nm) ± red (660 nm) light an effective and safe treatment for AV [10-12].

Aziz-Jalali MH, et al. showed that LLLT using 630-nm laser (red spectrum) significantly reduces active acne lesions after 12 sessions of treatment. They concluded that LLLT in red spectrum is a safe modality in treating facial AV without any complication [3].

There were no previous studies comparing split face treatment one side with LLLT alone and the other side with topical antibiotic alone. It is possible to use LLLT in combination with pharmacological treatment. There was one study demonstrating significant reduction in active acne lesions

after 12 sessions using 630-nm red LLLT with a fluence of 12 J/cm<sup>2</sup> twice a week for 12 sessions with 2% topical clindamycin [13]. A few studies also showed that the combination of blue and red light have synergistic effects in acne treatment [14].

In the current study, there was statistically significant improvement of papulopustular, nodulocystic and associated comedonal lesions on laser side. The papulopustular lesions showed a statistically highly significant value.

Szymańska A, et al. showed significant improvement in non-inflammatory and inflammatory lesion counts with no adverse effects reported with a LLL [15]. It is also worth mentioning that in most studies improvement in inflammatory lesions was higher than the improvement in comedones. The analysis of the effectiveness of the performed procedures was based on sebumetric examination, photographs and the change in the number of acne lesions [9].

Another study has also shown a positive interaction between light, specifically red, and the release of anti-inflammatory cytokines, which is one of the mechanisms in the pathogenesis of acne [16].

A well-controlled single-blind study compared mixed blue (415 nm) and red light (660 nm) with blue light alone. They were compared with cool white light and 5% BPO. The patients were with mild and mild/moderate acne. There was a significant difference between the white light group and other therapies; the combined blue-red light was generally better than blue light alone. The data for comedone counts

**Table 6. Comparison between laser and antibiotic side according to degree of improvement.**

Degree of Improvement	Laser side (N = 40)		Antibiotic side (N = 40)		MH	P
	N	%	N	%		
No	2	5.0	6	15.0	16.50	0.048
Fair	4	10.0	6	15.0		
Moderate	2	5.0	0	0.0		
Marked	2	5.0	6	15.0		
Excellent	30	75.0	22	55.0		

MH = Marginal Homogeneity Test.

**Table 7: Comparison between laser and antibiotic side according to side effects.**

Complications	Laser side (N = 40)		Antibiotic side (N = 40)		$\chi^2$	McNp
	N	%	N	%		
No	12	30.0	6	15.0	1.290	0.375
Yes	28	70.0	34	85.0		
Transient erythema	8	20.0	4	10.0	0.784	0.625
Pigmentation	14	35.0	8	20.0	1.129	0.375
Erythema and relapse	2	5.0	10	25.0	3.137	0.125
Relapse	0	0.0	12	30.0	7.059	0.031
Pigmentation and relapse	4	10.0	0	0.0	2.105	0.500
Relapse					MH	P
GEA					6.50*	0.020
I	34	85.0	18	45.0		
II	4	10.0	18	45.0		
III	2	5.0	2	10.0		
IV	No	No	No	No		
V	No	No	No	No		
IAA					6.50*	0.020
No	34	85.0	18	45.0		
Mild	4	10.0	18	45.0		
Moderate	2	5.0	4	10.0		

IAA = Indian Acne Association; GEA = Global Acne Severity; McN = McNemar test.



**Figure 1.** (A) 19-years old male patient with grade V acne showed marked improvement after 8 sessions of low-level laser and changed to grade I according to the global evaluation of acne scale; (B) The other side of the same patient with grade III acne showed moderate improvement with the topical antibiotic, and changed to grade II according to the global evaluation of acne scale; (C) After 3 months follow up, there was the maintenance of improvement on laser side and relapse with grade II on antibiotic side according to the global evaluation of acne scale.



**Figure 2.** (A) 21-years old male patient with grade IV acne showed excellent improvement after 8 sessions of low-level laser and changed to grade I according to the global evaluation of acne scale; (B) The other side of the same patient with grade IV acne showed fair improvement with topical antibiotic and changed to grade III according to the global evaluation of acne scale; (C) After 3 months follow up, there was the maintenance of improvement on laser side and relapse with grade IV on antibiotic side according to the global evaluation of acne scale.



**Figure 3.** (A) 18-years old female patient with grade V acne showed excellent improvement after 8 sessions of low-level laser and changed to grade I according to the global evaluation of acne scale; (B) The other side of the same patient with grade III acne showed excellent improvement with topical antibiotic and changed to grade I according to the global evaluation of acne scale; (C) After 3 months follow up, there was the maintenance of improvement on laser side and relapse with grade II on antibiotic side according to the global evaluation of acne scale.

showed a significant reduction occurred with active therapy and an increase in comedones in the control group [10].

In our study, there was improvement in severity of acne after treatment with antibiotic according to the GEA scale.

A study showed that erythromycin treatment (with zinc acetate) gel showed to be more effective than erythromycin gel (alone) with respect to reducing the number of acne lesions and severity of acne. Number of lesions and severity of acne were significantly reduced at the end of 3rd week in both groups [17]. This showed efficacy of antibiotic in AV treatment.

Topical antibiotics are thought to accumulate in the follicle and may work through both anti-inflammatory and antibacterial effects. Due to increasing antibiotic resistance,

monotherapy with topical antibiotics in the management of acne is not recommended. The main topical antibiotics are clindamycin and erythromycin [18].

Ross JI, et al. showed that the widespread use of topical erythromycin and clindamycin to treat acne has resulted in dissemination of cross-resistant strains of propionibacteria [19]. As bacterial antibiotic resistance continues to emerge as a serious global threat, it is crucial that all clinicians re-examine their use of antibiotics. The idea of “no more antibiotics for acne” should at least provoke thoughtful self-appraisal of current prescribing habits for many others [20].

Another study included 96 patients with mild to moderate AV who were treated with 2% alcoholic solution of

azithromycin, erythromycin and clindamycin respectively twice daily for 16 weeks. They reported that there was a statistically significant decrease in inflammatory lesions of acne and comedones with erythromycin treatment [21].

In the current study, our results showed that on laser side, 2 patient showed no improvement and 28 patients showed improvement in the form of: Fair improvement in 4 patients, moderate improvement in 2 patient, marked improvement in 2 patient and excellent improvement in 30 patients. On antibiotic side, 6 patients showed no improvement and 34 patients showed improvement in the form of: Fair improvement in 6 patients, marked improvement in 6 patients, and excellent improvement in 22 patients.

Moreover, the efficacy was investigated by using five antimicrobial regimens for mild to moderate facial acne and whether propionibacterium antibiotic resistance affects treatment response, 649 community participants were allocated one of five antibacterial regimens. The results revealed that 66% of patients expressed moderate or greater improvement at 18 weeks of treatment with topical erythromycin and BPO in a combined formulation [22].

A point of interest, some patients experienced improvement in skin texture and facial tightening with laser sessions. On laser side, patients were more satisfied than antibiotic side. Laser treatment has important advantage of low cost, no side effects, no daily twice application of creams and great efficacy with less relapse. This made our patients more satisfied with laser treatment than with topical antibiotic that caused irritation to some of them and bad compliance of others.

As regard side effects, the current study showed that on laser side, 12 patients showed no side effects and 28 patients experienced side effects in the form of erythema, pigmentation, and relapse. On antibiotic side, 6 patients showed no side effects, and 34 patients experienced side effects in the form of erythema, pigmentation, and relapse.

In a certain study, six patients discontinued their treatment because of undesirable results and experience of deterioration and discomfort, though none of the patients showed any harmful direct side effects from filtered light phototherapy such as burns, pigmented macules, keratosis etc. One patient dropped out after two sessions and the other three dropped out after four to five sessions because of unsatisfactory results as claimed by the patients themselves. Meanwhile, 2 patients refused from continuing the trial, as they did not like to use erythromycin due to undesirable smell and stinging sensation [23]. Side effects though minor includes erythema, peeling, itching, dryness, and burning [24].

Our study showed that laser treatment reduces relapse more than topical antibiotic.

Demina OM and Kartelishv AV, conducted their study to investigate the pathogenic importance of comorbidity for

acne recurrence and chronicity as well as to study effectiveness of LLLT. The patients were followed up for 1 year. The results showed a significant reduction in acne score at LLLT treated patients with mild to no recurrence [25].

Our results are compatible with a study that conducted a case control analysis to determine predictors of acne relapse (as defined by receiving an anti-acne medication). A second case-control analysis was performed to determine predictors of receiving a second isotretinoin treatment. The index date of cases was the calendar date of dispensing an anti-acne medication (isotretinoin or systemic antibiotics for 30 days including topical erythromycin, systematic erythromycin). Recurrence rate ratios were estimated using conditional logistic regression. The results showed that being male less than 16 years of age, receiving antibiotics showed greater relapse rate compared to those who received isotretinoin cumulative doses greater than 2450 mg and an isotretinoin treatment longer than 121 days [26].

Previous studies reported that LLLT can modulate acute inflammation and TNF $\alpha$  levels. LLLT appears to be critical for reducing TNF $\alpha$  release [27]. Also, it has the ability to reduce oxidative stress generated by reactive oxygen species [28].

Finally, treatment of inflammatory AV by laser showed great improvement in associated comedonal lesions. With laser treatment, some patients showed better skin texture and tightening of facial skin. Patients were more satisfied with laser treatment as it is safe, effective, cheap with relatively no side effects. Furthermore, laser reduces relapse greatly which is a great drawback of acne.

Treatment of inflammatory AV by laser and topical antibiotic was effective. Laser side showed more improvement than antibiotic side. There was improvement in papulopustular, nodulocystic and associated comedonal lesions. With laser treatment, some patients showed better skin texture and tightening of facial skin. Patients were more satisfied with laser treatment as it is safe, easy applicable and cheap with relatively no side effects, no daily twice application of creams and great efficacy. Laser treatment reduces relapse more than topical antibiotic.

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