

# Efficacy of intense pulsed light combined with topical erythromycin solution 2% versus topical erythromycin solution 2% alone in the treatment of persistent facial erythematous acne macules

Gita Faghihi, Amin Kharaziha Isfahani, Seyed Mohsen Hosseini<sup>1</sup>, Mohammad Reza Radan<sup>2</sup>

Department of Dermatology, Skin diseases and Leishmaniasis research center, Isfahan University school of medicine,

<sup>1</sup>Department of Biostatistics and Epidemiology, Skin diseases and Leishmaniasis research center, <sup>2</sup>Medical supervisory office of Vice chancellor of medical practice, Isfahan University of Medical sciences, Isfahan, Iran.

## Abstract

**Background:** There is always a necessity for newer acne treatments. Intense pulsed light (IPL) technology has been used for this purpose but there are limited studies in this field. As macular and erythematous remnants of acne inflammatory lesions are very common, resistant, and long lasting, we decided to evaluate the efficacy of IPL (as a tool for diminishing erythematous reactions in the tissues) for the treatment of residual erythematous macules following facial acne.

**Materials and Methods:** Thirty-five patients were registered in the study. Patient recruitment occurred between January 2010 and June 2011, and the study was completed in October 2011. Every patient received three IPL sessions, with a 2 week interval, on the right side of his/her face. Also, we recommended the patients to apply topical erythromycin solution 2% twice daily on their entire face from start to end of the study (i.e. until 3 months after the third IPL session). An independent physician counted the number of erythematous macules before every IPL session and 1 and 3 months after the last session.

**Results:** Thirty-three patients completed the study and were enrolled in analysis. Results of the study show that IPL therapy decreases the number of erythematous macules along the time.

**Conclusions:** IPL can accelerate the improvement rate of persistent erythematous macules remained after inflammatory acne subsides. More studies are needed to explain the exact role of it.

**Key words:** Facial acne, intense pulsed light, persistent erythematous macules, topical erythromycin solution 2%

## Address for correspondence:

Dr. Amin Kharaziha Isfahani, Skin and Stem Cell Research Center, Tehran University of Medical Sciences, Tehran, Iran, Dermatology department, Isfahan University School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran. E-mail: [amin.kharazi@yahoo.com](mailto:amin.kharazi@yahoo.com)

Received:09-01-2012, Accepted: 12-03-2012

## Access this article online

Quick Response Code:



Website:

[www.advbiores.net](http://www.advbiores.net)

DOI:

10.4103/2277-9175.102974

## INTRODUCTION

Acne vulgaris is a very common skin disease worldwide. It is associated with the high probability of adverse cosmetic and psychosocial effects. Even with the presence of various effective treatments, there is always necessity for nearly harmless, accessible, and most effective treatment options for acne.<sup>[1]</sup> The

Copyright: © 2012 Faghihi. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**How to cite this article:** Faghihi G, Isfahani AK, Hosseini SM, Radan MR. Efficacy of intense pulsed light combined with topical erythromycin solution 2% versus topical erythromycin solution 2% alone in the treatment of persistent facial erythematous acne macules. *Adv Biomed Res* 2012;1:70.

necessity to describe such complementary treatments is possibly forced by such topics as antibiotic resistance, and the side effects and monitoring supplies included by oral isotretinoin use.<sup>[2]</sup> Various light-related technologies have been assessed in the treatment of acne vulgaris, and hopeful initial results have been suggested by some investigators but their studies were mainly relatively small, uncontrolled case series.<sup>[3]</sup> Even with some predicted mechanisms whereby light-related technologies may improve acne vulgaris, exact confirmation of the efficacy of these methods is absent. Performing an analysis in the sources in this field will reveal a rarity of randomized, controlled experiments of laser and light-based treatments for acne vulgaris.<sup>[4]</sup> For that reason, we performed a randomized trial of intense pulsed light (IPL) via IPULSE™, for the treatment of persistent erythematous macules that remain after inflammatory lesions of facial acne and do not respond to routine therapies.

## MATERIALS AND METHODS

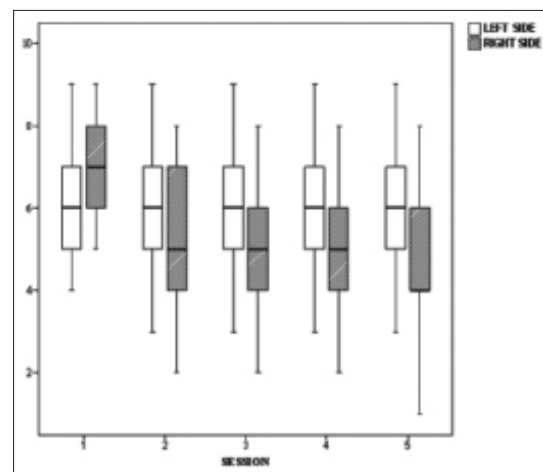
Thirty-five patients were registered in the study. Patient recruitment occurred between January 2010 and June 2011, and the study was completed in October 2011. In this study, inclusion criteria were the presence of at least five persistent erythematous acne macules on every side of the patients' face. The lesions should be persistent even with receiving at least 2 months of standard treatments. The patients were cases of mild to moderate facial acne vulgaris. Exclusion criteria were oral retinoid use from 6 months before the study, necessity of systemic treatments (i.e. nodulocystic or scarring acne), history of keloid, vitiligo, consumption of drugs that exacerbate or remit acne lesions, history of skin cancer, photosensitivity disorders, and history of poor wound healing such as diabetes mellitus. Patients were invited to discontinue both oral and topical acne treatments at least 4 and 2 weeks, respectively, before first IPL session and also during the study (i.e. until 3 months after the third IPL session). Our patients were employed from dermatology clinics at Isfahan University of Medical Sciences. Our study was a randomized, single-blind clinical trial. Case and control groups were right and left sides of face, respectively. Every patient received three IPL sessions, with a 2 week interval, on right side of his/her face. Also, we recommended the patients to apply topical erythromycin solution 2% (Pakdaru, Iran) twice daily on their entire face from start to end of the study (i.e. until 3 months after third IPL session). Before every IPL session, patients were requested to eliminate all makeup and wash their face with soap and water. All IPL treatments were performed by IPULSE™ system with the ensuing parameters: 530-1100 nm

wavelength, 33 mm× 27 mm spot size, and one pass was given with an average fluence of 14-16 J/cm<sup>2</sup>. The system pulse duration is computer controlled as various programs. In our study, administered programs were 14-18. We recommended all patients to avoid sun exposure for 48 h and regularly apply oil-free SPF 30 sunscreen (Rassen, Iran) and oil-free moisturizer (Dr Jila, Iran). An independent physician evaluated the patients clinically before every IPL session, and one and 3 months after the third session. He properly counted the number of erythematous macules using photos and also clinically by examination of the patients face. An amateur photographer took the facial photos using a digital camera (1024×768 pixels), before every IPL session, and 1 and 3 months after the third session. Left and right views were taken. The non-treating dermatologist was blinded with regard to which side of the faces was treated by IPL. In addition, our patients were evaluated 1 week after every IPL session for potential severe side effects. Right and left sides of face were recorded separately. We applied repeated measures ANOVA and Mauchly's test of sphericity for data analysis. We utilized the SPSSv15 software for this purpose.

## RESULTS

Fifty-four patients were screened and 35 patients were found to meet all eligibility criteria and were thus enrolled in the study. Thirty-three patients including 8 males and 25 females with an average age of 24 ±2.5 years and the range of 16-42 years completed the study and included in analysis. None of the patients evolved to nodulocystic acne. Regarding skin phototype (Fitzpatrick) patients were included: Phototype 2 (9 patients), phototype 3 (24 patients), phototype 4 (2 patients).

At first, we utilized the BOXPLOT diagram for mean



**Figure 1:** Boxplot diagram for mean number of erythematous macules on both sides of face

**Table 1: The means and standard deviations of the number of erythematous macules**

|       | Baseline    | Before the second IPL session | Before the third IPL session | One month after the third PL session | Three months after the third IPL session |
|-------|-------------|-------------------------------|------------------------------|--------------------------------------|--|
| Right | 6.82 ± 1.28 | 5.33 ± 1.55                   | 5.21 ± 1.51                  | 4.48 ± 1.56                          | 4.82 ± 1.40                              |
| Left  | 6.30 ± 1.35 | 6.27 ± 1.54                   | 6.15 ± 1.43                  | 6.09 ± 1.48                          | 6.06 ± 1.58                              |

**Table 2: Repeated measures analysis of variance summary table**

| Source               | SS      | df  | F      | P      |
|----------------------|---------|-----|--------|--------|
| Time (session)       | 64.312  | 4   | 26.676 | <0.001 |
| Treatment(side)*Time | 42.982  | 4   | 17.827 | <0.001 |
| Residual             | 154.303 | 256 |        |        |

**Table 4: Significant side effects of the treatment**

|                  | One week after first IPL session |       | One week after second IPL session |       | One week after third IPL session |       |
|------------------|----------------------------------|-------|-----------------------------------|-------|----------------------------------|-------|
|                  | Left                             | Right | Left                              | Right | Left                             | Right |
|                  | Severe pain                      | 1     | 4                                 | 0     | 0                                | 0     |
| Severe erythema  | 1                                | 4     | 0                                 | 2     | 0                                | 2     |
| Photosensitivity | 1                                | 2     | 0                                 | 2     | 0                                | 1     |
| Severe swelling  | 1                                | 1     | 0                                 | 0     | 0                                | 0     |
| Blister          | 0                                | 0     | 0                                 | 0     | 0                                | 0     |
| Severe crusting  | 1                                | 1     | 0                                 | 0     | 0                                | 0     |

number of erythematous macules in consecutive treatment sessions, for both sides of face. We can see a decreasing pattern in the number of erythematous macules on the right side (i.e. IPL treated side). Please see the diagram in Figure 1.

Also, the mean number of erythematous macules in consecutive treatment sessions for both sides of the face is presented in Table 1.

For data analysis, we utilized the repeated measures analysis of variance (repeated measures ANOVA). Results of the analysis are presented in Table 2. We used WILKS LAMBDA statistic value to test the effectiveness of the therapeutic method in consecutive treatment sessions. The quantity of this value was 0.525 and therefore was statistically significant at the level of 5% ( $P < 0.001$ ) and revealed that the changes of the number of erythematous macules on the right side are different from the left side. Mauchly's test of sphericity revealed trespass of the model from sphericity provision ( $P < 0.001$ ) and therefore we applied the adjustment of Greenhouse-Greisser's degree of freedom for meaningful evaluation of time effect and reciprocal effect of time and treatment. Results shown that both the time effect and the reciprocal effect of time and treatment were statistically significant at the level of 5% ( $P < 0.001$ ). So, the test rejected that IPL therapy has been non-effective and results of the study show that IPL therapy decreases the number of erythematous macules along the time.

**Table 3: Test of between-subjects effects**

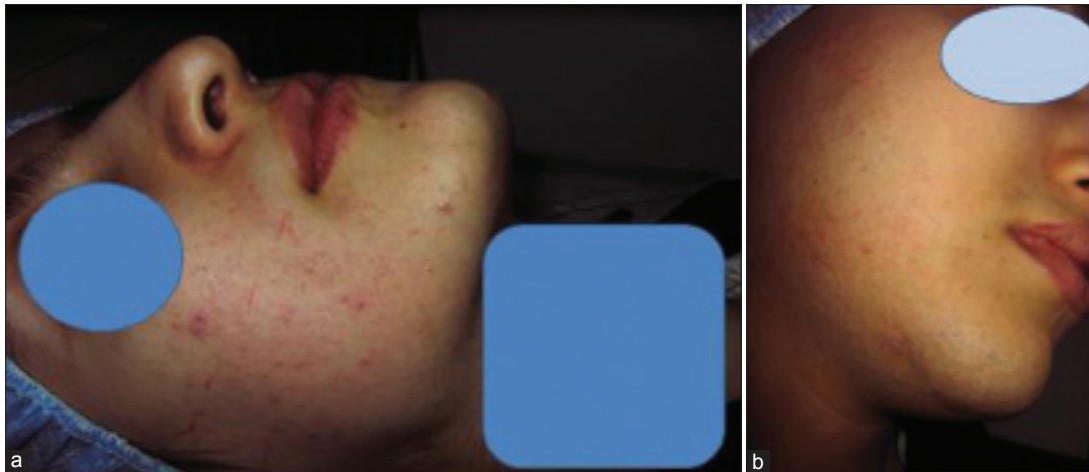
| Source    | Type 3 sum of squares | df | Mean square | F        | Sig   | Partial eta squared |
|-----------|-----------------------|----|-------------|----------|-------|---------------------|
| Intercept | 10927.88              | 1  | 10927.88    | 1288.073 | 0     | 0.953               |
| Side      | 58.548                | 1  | 58.548      | 6.901    | 0.011 | 0.097               |
| Error     | 542.97                | 64 | 8.484       |          |       |                     |

Also, degree of difference between right and left sides (i.e. case group versus control group) was statistically significant at the level of 5% ( $F(1,64)=6.901$ ,  $P=0.011$ ,  $\eta^2=0.097$ ). Table 3.

Although 35% of the patients reported mild burning and erythema on IPL-treated side (lasted only a few hours), four patients developed significant pain and erythema (more than 1 day). We treated them by supportive treatments including sunscreen and emollient. However, two cases did not tolerate the condition and voided the study. One of these two patients developed severe bilateral pain, erythema, swelling, crusting, and photosensitivity [Table 4]. Almost 10% of the patients reported mild burning on both sides of their face due to application of topical erythromycin lotion.

## DISCUSSION

The reasons for use of IPL in the treatment of erythematous macules that remain after inflammatory lesions of facial acne may be properties of the inflammatory lesions. These lesions are characterized by response of vasodilation due to inflammatory Process resulting in collection of abundant red blood cells and generated photothermal reactions resulting in improvement and reduction of inflammatory acne lesions.<sup>[5]</sup> IPL therapy aim and damage the skin bacteria responsible for acne and may prevent potential breakouts of acne vulgaris.<sup>[6]</sup> The pulsed light technology provides correct quantities of light in the proper spot sizes for the patients treatment needs. IPL eradicates the bacteria and gently heats up the skin around the spots and subsequently produces collagen that enhances the healing process. Some investigators suggest that the mechanisms of blue and red light work synergistically to induce a response. The treatment often takes less than 30 min. Results are typically seen within 2 weeks with continued improvement over the ensuing 3 months. The patient



**Figure 2:** (a) Before start of trial. On this side she should be given IPL. (b) Three months after the end of treatment with IPL.

may apply moisturizer immediately and return to work or other activities. He/she should see results from the recommended treatment protocol in 90 days. The IPL system releases yellow, green, and red light that is emitted in a sequence of short pulses. The yellow/green light damages the bacteria that live in the skin and cause acne, while the red light directly aims the overactive sebaceous glands that cause outbreaks of pustules. This targeted heating, deep in the skin, causes shrinkage of the inflamed sebaceous glands and helps to prevent over-production of excess sebum.<sup>[7]</sup>

Rojanamantin and Choawawanich demonstrated that IPL both alone and following 5-ALA application can improve inflammatory facial acne but the degree improvement was better on the 5-ALA pretreated sides.<sup>[8]</sup>

Yeung *et al.* investigated the reaction of IPL on Asian skin. It often differs from the reaction of IPL on Caucasian skin. They found significant reductions of non-inflammatory lesions in the IPL-treated group 12 weeks after treatment, but IPL did not lead to significant improvement of moderate inflammatory acne compared with the control group.<sup>[9]</sup>

In a review, Haedersdal and colleagues identified results of 16 randomized controlled trial (RTC) and 3 controlled trial (CT), about laser and light sources in treatment of acne vulgaris, included IPL (1RCT and 2CTs). IPL assisted photodynamic therapy seems to be superior to IPL alone.<sup>[10]</sup>

Sami and Attia investigated phototherapy in the treatment of acne vulgaris because of the increase in antibiotic resistance. In their study, a mean of  $6 \pm 2.05$  IPL sessions was required to achieve more than 90% clearance of inflammatory lesions.<sup>[11]</sup>

We found a statistically significant decrease in the mean number of erythematous macules on IPL treated side along the time. The reduction continued at least 3 months after the third IPL session [Figure 2]. Our results is compatible with the results of Rojanamantin but was different from the findings of Yeung study. This may be due to difference in the reaction of skin to IPL therapy between Caucasians and Asians. In our study, only four patients developed significant erythema and burning following IPL therapy and two of them voided the study. We did not find any case of blister or pigmentation disturbances following IPL therapy. Additional side effects due to IPL or topical erythromycin lotion were trivial and tolerable.

## CONCLUSION

Briefly, our study adopted some previous trials that demonstrated the IPL technique as an effective and safe therapeutic method for the treatment of inflammatory lesions of facial acne. While previous studies evaluated this method for early inflammatory macules, papules, and pustules, we tested IPL therapy for persistent erythematous macules. The beneficial effect remained at least 3 months after the last IPL session. However, more studies are necessary to define the correct role of IPL in the treatment of various lesions of facial acne.

## ACKNOWLEDGMENTS

We are grateful to the dear staff of Sadaf Skin and hair transplantation center and the staff of Skin and hair clinic of Alzahra Hospital.

## REFERENCES

1. Goldman MP, Boyce SM. A single center study of aminolevulinic acid and 417 nm photodynamic therapy in the treatment of moderate to severe acne vulgaris. *J Drug Dermatol* 2003;2:393-6.

Faghihi, *et al.*: Efficacy of intense pulsed light in the treatment of persistent facial erythematous acne macules

2. Warren RH. Intense pulsed light. *J Am Acad Dermatol* 2007;56:466-7.
3. Santos MA, Belo VG. Effectiveness of photodynamic therapy with topical 5-aminolevulinic acid and intense pulsed light versus intense pulsed light alone in the treatment of acne vulgaris. *Dermatol Surg* 2005;31:910-5.
4. Mariwalla K, Rohrer T. Use of lasers and light-based therapies for treatment of acne vulgaris. *Lasers Surg Med* 2005;37:333-42.
5. Chang SE, Ahn SJ, Rhee DY. Treatment of facial acne papuls and pustules in Korean patients using an intense pulsed light device equipped with a 530 to 750 nm filter. *Dermatol Surg* 2007;33:676-9.
6. Taub AF. A comparison of intense pulsed light, combination radiofrequency and intense pulsed light and blue light in photodynamic therapy for acne vulgaris. *J Drugs Dermatol* 2007;6:1010-6.
7. Torres V, Torezan L. Light based therapies for skin of color. London: Springer; 2009. p. 249-61.
8. Rojanamatin J, Chowawanich P. Treatment of inflammatory acne vulgaris with intense pulsed light and short contact of topical 5-aminolevulinic acid: A pilot study. *Dermatol Surg* 2006;32:991-6.
9. Yeung CK, Shek SY, Bjerring P. A comparison study of intense pulsed light alone and its combination with photodynamic therapy for the treatment of facial acne in Asian skin. *Laser Surg Med* 2007;39:1-6.
10. Haedersdal M, Togsversd K, Wulf HC. Evidence based review of laser, light sources and photodynamic therapy in treatment of acne vulgaris. *J Eur Dermatol Venereal* 2008;22:267-78.
11. Sam NA, Attia AT, Badawi AM. Phototherapy in the treatment of acne vulgaris. *J Drugs Dermatol* 2008;7:627-32.

**Source of Support:** Isfahan university of medical sciences. **Conflict of Interest:** None declared.