

# The Efficacy of Intense Pulsed Light for Treating Erythematotelangiectatic Rosacea Is Related to Severity and Age

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**Background:** Rosacea is a chronic cutaneous disease. Therapeutic modalities should be chosen based on the identified sub-types and clinical features in each patient. Vascular lasers, including intense pulsed light (IPL), are reportedly safe and effective in treating erythematotelangiectatic rosacea (ETR). **Objective:** In this study, we assess the comparative efficacy of IPL related to several factors including clinical severity and the age of patients with ETR. **Methods:** Patients with ETR were classified into two groups according to the National Rosacea Society Severity Guideline. Severity score and erythema index (EI) were measured using a clinical scorecard and mexameter. For additional evaluation of therapeutic efficacy, investigator and patient global assessments (IGA, PGA) were checked. Efficacy of IPL was analyzed according to severity score, EI, IGA, and PGA related to sex, age, lactic acid stinging test, and severity. **Results:** Analyses of the efficacy of IPL according to severity score, EI, IGA, and PGA based on sex, age, lactic acid stinging test, and severity revealed significant differences with age and severity only. **Conclusion:** This study supports the efficacy of IPL treatment for patients with ETR. IPL may be more effective in patients with more severe ETR and in younger patients with ETR. (*Ann Dermatol* 26(4) 491 ~ 495, 2014)

## -Keywords-

Age factors, Intense pulsed light therapy, Rosacea

## INTRODUCTION

Rosacea is a chronic cutaneous disease that manifests as facial flushing, persistent erythema, telangiectasia, papules, and pustules; it typically involves the central facial region. There are four rosacea sub-types: erythematotelangiectatic, papulopustular, phymatous, and ocular<sup>1,2</sup>. Erythematotelangiectatic rosacea (ETR) is the most common and may have the strongest vascular component among the four sub-types<sup>2</sup>. Although traditional antibiotic therapy usually improves papulo-pustular lesions, vascular components are often persistent<sup>3</sup>. Several studies have demonstrated the successful use of intense pulsed light (IPL) for the vascular components of ETR, including facial telangiectasia<sup>4-7</sup>. However, little is known of the link between the efficacy of IPL and several factors including severity, age, sex, and location. This study assessed factors affecting the efficacy of IPL in patients with ETR.

## MATERIALS AND METHODS

### Patients

Fifty patients with ETR were retrospectively recruited from patients visiting Chonnam National University Hospital (Gwangju, Korea) from July 2009 to December 2012. Patients who had previously received laser treatments for rosacea were excluded. Severity was measured based on the National Rosacea Society Expert Committee's guidelines for ETR symptoms: flushing (transient erythema), nontransient erythema, telangiectasia, burning or stinging,

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**Table 1.** Demographic characteristic of patients with ETR according to severity

	Mild group	Moderate/severe group
Mean age (yr)*	50.17	48.5
Sex†	35	15
Male	15 (42.9%)	4 (26.7%)
Female	20 (57.1%)	11 (73.3%)
Severity score (mean)	7.49	16.67
Lactic acid stinging test (positive reaction)‡	38.1%	42.8%

ETR: erythematotelangiectatic rosacea. Mild group (range, 0~9), moderate group (range, 10~18), severe group (range, 19~27). \* $p=0.077$ , †male to female ratio:  $p=0.082$ , ‡ $p=0.162$ ; analysis of Wilcoxon rank sum test.

plaques, dry appearance, edema, physician’s global assessment and patient’s global assessment. Scores from 0~3 (0, absent; 1, mild; 2, moderate; 3, severe) were assigned to each category and patients were divided into mild (range, 0~9), moderate (10~18), and severe (19~27) groups. Since the number of patients in the moderate group ( $n=10$ ) and the severe group ( $n=5$ ) were relatively small compared to that of the mild group ( $n=35$ ), the first two were combined into the moderate/severe group (Table 1)<sup>8,9</sup>.

**IPL treatment**

The IPL source used was a Rex-Prime model (Union Medical, Uijeongbu, Korea). A 560 nm cut-off filter was used. Treatment energy ranged from 12~16 J/cm<sup>2</sup> and pulse duration ranged from 6~7 msec. A total of four treatments were administered to the whole face at 3-week intervals. After each treatment session, all patients were instructed to use broad-spectrum sunscreen on a daily basis and to use proper photoprotection.

**Efficacy evaluation**

Severity scores were measured again after the four treatment sessions. Using a model MX18 mexameter (CK Electronic GmbH, Cologne, Germany), the erythema index (EI) of the forehead, cheeks, nose, and chin was measured before and after treatment. Clinical photographic images before and after treatment were compared by three physicians. Treatment efficacy was evaluated using the investigator global assessment (IGA) 4-point scale (1, poor; 2, fair; 3, good; 4, excellent). The mean of three scores was used. For subjective evaluation, patient satisfaction after treatment was assessed with the patient global assessment (PGA) 4-point scale (1, <25%; 2, 25~50%;

**Table 2.** Demographic characteristics of patients with ETR according to age

	≤40 yr	>40 yr
Mean age (yr)	31.1	59.8
Sex*	21	29
Male	10 (47.6%)	9 (31.0%)
Female	11 (52.4%)	20 (69.0%)
Severity score (mean)†	10.71	10.06
Lactic acid stinging test (positive reaction)‡	39.1%	39.8%

ETR: erythematotelangiectatic rosacea. \*Male to female ratio:  $p=0.091$ , † $p=0.493$ , ‡ $p=0.102$ ; analysis of Wilcoxon rank sum test.

3, 50~75%; 4, >75%). Each patient was assessed with a lactic acid stinging test—application of 5% lactic acid solution on both nasolabial folds. After 2, 5, and 10 min, the presence of stinging, itching, or burning on both sides was determined (Table 1, 2). For each visit, patients were queried concerning any occurrence of adverse events. SPSS Statistics version 17.0 (SPSS Inc., Chicago, IL, USA) was used for all comparative analysis related to several factors. To assess IPL efficacy, the difference of severity score and EI before and after treatment, severity score and EI after treatment, IGA, and PGA were compared between the mild and moderate/severe groups. To identify factors that influenced IPL efficacy other than severity (sex and positive reaction in the lactic acid stinging test) all patients were also grouped into two age groups (≤40 and >40 years old) (Table 2). The Wilcoxon rank sum test was used to examine statistical differences in demographics between the two age groups and two severity groups. Finally, these groups were analyzed via the same test for IPL efficacy.

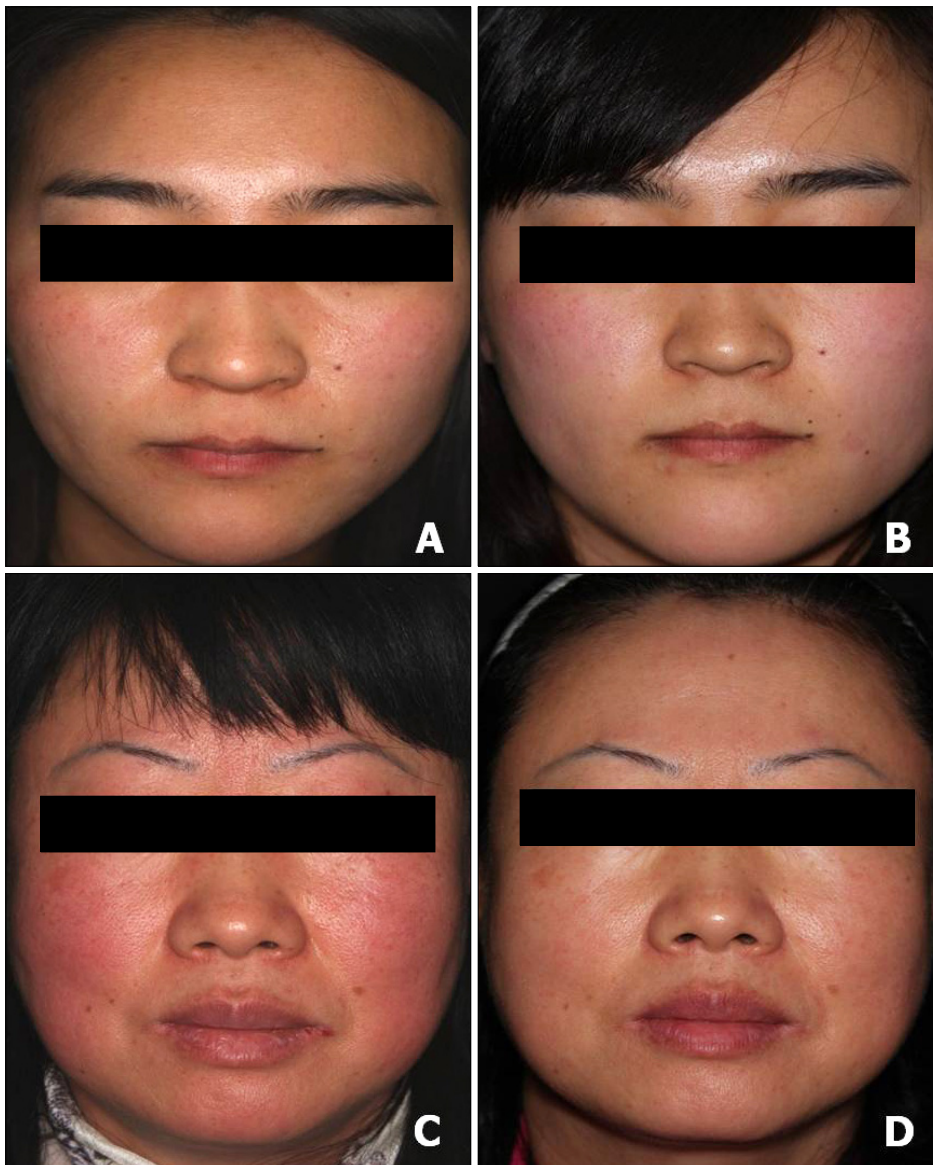
**RESULTS**

Analyses of differences in the efficacy of IPL based on sex, age, lactic acid stinging test results, and severity revealed significant relationships with age and severity only. Differences in severity scores (3.63 vs. 12.67,  $p=0.004$ ) and EI (43.13 vs. 73.92,  $p=0.017$ ) between pre-treatment and post-treatment were significantly greater in the moderate/severe group than in the mild group (Table 3, Fig. 1). Similarly, patients ≤40 years old had significantly different severity scores (7.85 vs. 5.75,  $p=0.026$ ) and EI (67.37 vs. 44.22,  $p=0.031$ ) between pre-treatment and post-treatment assessments (Table 3). Differences in IGA (severity group,  $p=0.042$ ; age group,  $p=0.044$ ) and PGA ( $p=0.016$ , 0.029) were also significant in the same groups (Table 3). However, for the post-treatment scores, there was no

**Table 3.** Summary of the results of IPL treatment according to the classified groups in patients with ETR

	Severity			Age (yr)		
	Mild	Moderate to severe	<i>p</i> -value	≤40	>40	<i>p</i> -value
Severity score						
Pre-treatment	7.49	16.67	0.021*	10.71	10.06	0.493
Post-treatment	3.86	4	0.281	2.86	4.31	0.041*
Δ(delta) <sup>†</sup>	3.63	12.67	0.004*	7.85	5.75	0.026*
Erythema index <sup>‡</sup>						
Pre-treatment	1,037.93	1,067.13	0.048*	1,045.91	1,046.99	0.562
Post-treatment	994.8	993.21	0.564	978.54	1,002.77	0.034*
Δ(delta) <sup>†</sup>	43.13	73.92	0.017*	67.37	44.22	0.031*
IGA	2.29	3.53	0.042*	3.07	2.5	0.044*
PGA	2.54	3.27	0.016*	3.64	2.42	0.029*

IPL: intense pulsed light, ETR: erythematotelangiectatic rosacea, IGA: investigator global assessment, PGA: patient global assessment. \*Statistically significant difference between two groups. <sup>†</sup>Difference between pre-treatment and post-treatment score. <sup>‡</sup>Mean value of forehead, cheek, nose and chin.



**Fig. 1.** Clinical photographic images of mild and moderate/severe groups. Mild group: (A) pre-treatment severity score 5, EI 1,021.92; (B) post-treatment severity score 5, EI 1,020.08, IGA1, PGA 2. Moderate/severe group: (C) pre-treatment severity score 25, EI 1,076.86; (D) post-treatment severity score 5, EI 988.86, IGA 4, PGA 4. EI: erythema index, IGA: investigator global assessment, PGA: patient global assessment.

difference in severity (3.86 vs. 4,  $p=0.281$ ) and EI (994.8 vs. 993.21,  $p=0.564$ ) between the mild group and the moderate/severe group. Furthermore, patients with ETR  $\leq 40$  years old also had significantly improved post-treatment severity scores (2.86 vs. 4.31,  $p=0.041$ ) and EI (978.54 vs. 1,002.77,  $p=0.034$ ) compared to patients  $> 40$  years old. Positive reaction in the lactic acid stinging test was displayed by 43.3% of patients with ETR. However, there was no significant difference in IPL efficacy in relation to sex or lactic acid stinging test results. Concerning side effects, four of 50 patients complained of erythema, six of pain during treatment, and one of hyperpigmentation.

## DISCUSSION

Rosacea is a typical cutaneous disease that can cause not only physical but also emotional distress due to many severe symptoms<sup>10,11</sup>. Therefore, choosing the proper therapeutic option for each patient is critical. For ETR, which presents with erythema and telangiectasia as primary symptoms, a combination of oral antibiotics, oral/topical therapy, and lasers are used for treatment. With long-term use of antibiotics, such as tetracycline, ampicillin, metronidazole, and erythromycin, side effects like gastrointestinal symptoms, photosensitivity, candida vaginitis, and reduction in oral contraceptive efficacy can occur. In case of extensive skin lesions, the therapeutic effect of topical therapy can be insufficient. Laser treatments, such as pulsed dye laser (PDL), which is commonly used for vascular lesions, and IPL, which is effective and safe, are proven alternatives<sup>12</sup>. Particularly, IPL penetrates the skin deeper than PDL and targets multiple chromophores at varying depths, including melanin and hemoglobin. Additional advantages of IPL include less down time, lower purchase price, mild adverse reactions, high versatility, high skin coverage rate, and shortened duration of treatment due to the large application area<sup>4,13</sup>. A randomized, controlled, single-blind split-face trial of PDL and IPL conducted with 29 patients with ETR demonstrated no significant difference in efficacy<sup>14</sup>.

The present study is the first trial to evaluate the severity-related, comparative efficacy of IPL treatment for ETR. When changes in parameters before and after treatment were analyzed, all four parameters demonstrated significant differences between the mild group and the moderate/severe group. Such results are considered to be related to the pathogenesis of rosacea. ETR is a process in which vessels are dilated due to genetic and environmental factors, causing extravascular leakage of inflammatory mediators, resulting in an inflammatory response<sup>1,2</sup>.

Thus, patients with severe symptoms have more abnormally dilated vessels (i.e. high vascular instability) making IPL, which mainly targets abnormal vessels, more effective in treating patients with greater vascular involvement. Although the differences in the parameters between pre-treatment and post-treatment were significant, there was no significant difference in the severity score between the two groups after treatment (Table 3). Thus, after sufficient IPL treatment, clinical features and symptoms of the mild and moderate/severe groups did not differ significantly. The results also demonstrate the need for additional therapeutic approaches to factors other than vascular instability, as well as the identification of other pathophysiological processes for complete remission of rosacea. Schroeter et al.<sup>7</sup> carried out IPL treatments on 60 patients with rosacea; the patient group had a mean age of 44.2 years (range 32~67) and a Pearson correlation yielded a  $p$ -value of 0.719, making the correlation between age and IPL efficacy statistically insignificant. In addition, Campolmi et al.<sup>15</sup> used IPL treatment on 63 patients with vascular lesions; the patient group had a mean age of 51.5 years (range 28~75 years) and was classified into three groups according to age (20~39/40~59/68~73 years). The efficacy was evaluated according to the following categories: slight, moderate or marked improvement. Analysis revealed that there was no difference in efficacy between the three age groups. The present study compared only the percentage of each group without statistical analysis. However, we divided the patients into two groups, using the age of forty as a discrete variable (under 40 years vs. over 40 years). These two categories account for the periods when rosacea may occur most commonly and when people begin photoaging, respectively. The result of this study revealed a better treatment response in patients  $< 40$  years old than in those  $> 40$  years old. Loss of mechanical integrity in the dermal matrix due to solar damage during aging is an important contributor to the acquisition of ETR<sup>16</sup>. Thus, in treating ETR, the recovery of such degenerative dermal tissue is essential. For instance, Li et al.<sup>17</sup> reported that IPL treatment increases the content of dermal collagen and elastic fiber in a split-face study. The mechanism for this is selective absorption of light by tissue water leading to the conduction of heat to the surrounding collagen, resulting in subsequent collagen synthesis<sup>18</sup>. Another mechanism involves the photothermal effect to induce synthesis of collagen I and III by increasing fibroblast activity<sup>19,20</sup>. It is hypothesized that patients  $< 40$  years old experience greater efficacy because aging is closely related to tissue water content and fibroblast activity, which are key factors in IPL treatment. The study was limited by the lower number of patients in

the moderate/severe group compared to the mild group and the relatively low rate of moderate/severe ETR. Additionally, an effective period or relapse time, depending on severity and age, needs to be determined through further investigation. Finally, this study was performed retrospectively.

In conclusion, IPL is confirmed to have sufficient therapeutic efficacy for patients with ETR without causing notable side effects. Therapeutic efficacy could be maximized if IPL is applied in patients with ETR that is moderate to severe and in those < 40 years old.

## REFERENCES

- Pell MT. Rosacea. In: Goldsmith LA, Katz SI, Gilchrist BA, Paller AS, Leffell DJ, Wolff K, editors. Fitzpatrick's dermatology in general medicine. 8th ed. New York: McGraw-Hill, 2012:918-925.
- Crawford GH, Pelle MT, James WD. Rosacea: I. etiology, pathogenesis, and subtype classification. *J Am Acad Dermatol* 2004;51:327-341.
- Bonnar E, Eustace P, Powell FC. The Demodex mite population in rosacea. *J Am Acad Dermatol* 1993;28:443-448.
- Babilas P, Schreml S, Szeimies RM, Landthaler M. Intense pulsed light (IPL): a review. *Lasers Surg Med* 2010;42:93-104.
- Papageorgiou P, Clayton W, Norwood S, Chopra S, Rustin M. Treatment of rosacea with intense pulsed light: significant improvement and long-lasting results. *Br J Dermatol* 2008;159:628-632.
- Kassir R, Kolluru A, Kassir M. Intense pulsed light for the treatment of rosacea and telangiectasias. *J Cosmet Laser Ther* 2011;13:216-222.
- Schroeter CA, Haaf-von Below S, Neumann HA. Effective treatment of rosacea using intense pulsed light systems. *Dermatol Surg* 2005;31:1285-1289.
- Wilkin J, Dahl M, Detmar M, Drake L, Liang MH, Odom R, et al; National Rosacea Society Expert Committee. Standard grading system for rosacea: report of the National Rosacea Society Expert Committee on the classification and staging of rosacea. *J Am Acad Dermatol* 2004;50:907-912.
- Wilkin J, Dahl M, Detmar M, Drake L, Feinstein A, Odom R, et al. Standard classification of rosacea: Report of the National Rosacea Society Expert Committee on the Classification and Staging of Rosacea. *J Am Acad Dermatol* 2002;46:584-587.
- Aksoy B, Altaykan-Hapa A, Egemen D, Karagöz F, Atakan N. The impact of rosacea on quality of life: effects of demographic and clinical characteristics and various treatment modalities. *Br J Dermatol* 2010;163:719-725.
- Bae YI, Yun SJ, Lee JB, Kim SJ, Won YH, Lee SC. Clinical evaluation of 168 Korean patients with rosacea: the sun exposure correlates with the erythematotelangiectatic subtype. *Ann Dermatol* 2009;21:243-249.
- van Zuuren EJ, Gupta AK, Gover MD, Graber M, Hollis S. Systematic review of rosacea treatments. *J Am Acad Dermatol* 2007;56:107-115.
- Kawana S, Ochiai H, Tachihara R. Objective evaluation of the effect of intense pulsed light on rosacea and solar lentigines by spectrophotometric analysis of skin color. *Dermatol Surg* 2007;33:449-454.
- Neuhaus IM, Zane LT, Tope WD. Comparative efficacy of nonpurpuragenic pulsed dye laser and intense pulsed light for erythematotelangiectatic rosacea. *Dermatol Surg* 2009;35:920-928.
- Campolmi P, Bonan P, Cannarozzo G, Brusolino N, Troiano M, Prignano F, et al. Intense pulsed light in the treatment of non-aesthetic facial and neck vascular lesions: report of 85 cases. *J Eur Acad Dermatol Venereol* 2011;25:68-73.
- James WD, Berger TG, Elston DM. *Andrews' diseases of the skin*. 11th ed. Philadelphia: Elsevier Saunders, 2011:241-244.
- Li YH, Wu Y, Chen JZ, Zhu X, Xu YY, Chen J, et al. A split-face study of intense pulsed light on photoaging skin in Chinese population. *Lasers Surg Med* 2010;42:185-191.
- Rokhsar CK, Lee S, Fitzpatrick RE. Review of photorejuvenation: devices, cosmeceuticals, or both? *Dermatol Surg* 2005;31:1166-1178.
- Liu H, Dang Y, Wang Z, Chai X, Ren Q. Laser induced collagen remodeling: a comparative study in vivo on mouse model. *Lasers Surg Med* 2008;40:13-19.
- Omi T, Kawana S, Sato S, Honda M. Ultrastructural changes elicited by a non-ablative wrinkle reduction laser. *Lasers Surg Med* 2003;32:46-49.