

## A Prospective Split-Face Comparative Study of Periorbital Wrinkle Treatments: Fractional Erbium-Doped Yttrium Aluminum Garnet Laser, Intense Pulsed Light, and Topical 0.1% Tretinoin Cream

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## Dear Editor:

Periorbital wrinkles are an early sign of skin aging, which can be of concern to relatively young adults. A variety of modalities has been used to treat periorbital wrinkles, including topical retinoid and glycolic acid preparations, botulinum and collagen injections, laser therapy, phototherapy, and nutritional therapy<sup>1</sup>. However, there are few studies that have compared the effectiveness and safety of treatments with different modalities<sup>2</sup>. Here, we designed a split-face study to compare the efficacy and safety of topical 0.1% tretinoin cream, nonablative nonlaser intense pulsed light (IPL), and fractional erbium-doped yttrium aluminum garnet (Er:YAG) laser for improving periorbital wrinkles. Nineteen Korean female participants aged between 30 and 52 years (mean age, 39.41 ± 5.51 years) were enrolled, and the Institutional Review Board of Kangwon Medical Center approved the study (IRB no. KNUH-2013-10-010-002). All participants applied 0.1% tretinoin cream on the right periorbital wrinkles once daily at night for 3 months. Fractional ablative treatment was carried out in 9 patients on the left periorbital wrinkles using a 2,940-nm Er:YAG laser (ACTION<sup>TM</sup>; Lutronic, Goyang, Korea); 10 J/cm<sup>2</sup>, 3 micropulse, 3 total treatments, 4-week intervals. The other 10 patients received IPL (SOLARITM; Lutronic) on the left periorbital wrinkles; 510 nm cutoff filter, 15 ms pulse interval, 13 J/cm<sup>2</sup>, 3 total treatments,

4-week intervals. Standardized digital photographs (Canon EOS 550D) were taken from the participants' bilateral periorbital wrinkles with the eyes lightly closed before treatment (baseline), monthly, and at 1 month after the last treatment (week 12). Blinded evaluation of the efficacy of each treatment was performed at week 12 by 5 independent dermatologists who assessed pre- and post treatment digital photographs. Eight-grade wrinkle scoring with increments of 0.25 used in this study has been authorized by the Japan Cosmetic Industry Association (Task Force Committee for Evaluation of Anti-Aging Function, J Jpn Cosmet Sci Soc 2007;31:411 ~ 431) (Fig. 1). We compared the degree of wrinkle improvement between baseline and at 1 month after the final session for the right and left treatment sides. Fig. 2 shows two participants' improvement from baseline to week 12. At week 12, mean wrinkle score on the IPL-treated side decreased by 20.4%, from 2.30 to 1.83, while that on the 0.1% tretinoin cream-applied side decreased by 21.0%, from 2.80 to 2.21. Mean wrinkle score on the Er:YAG laser-treated side decreased by 20.0%, from 2.00 to 1.60, while that on the 0.1% tretinoin cream-applied side decreased by 26.8%, from 2.31 to 1.69. However, there was no significant difference in degree of wrinkle improvement among the 3 modalities. Seven of 19 participants experienced adverse effects of tretinoin cream, which included erythema, burning sensa-

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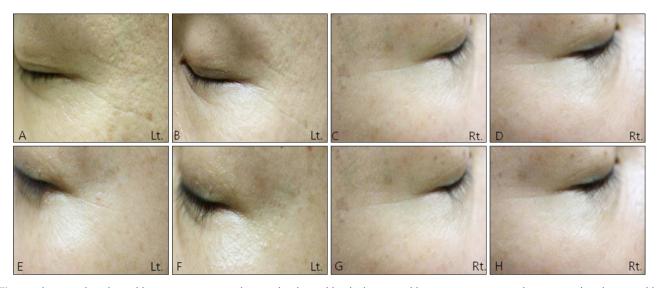
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Fig. 1. Eight-grade wrinkle scoring according to the Japan Cosmetic Industry Association. Reprinted from the article of Task Force Committee for Evaluation of Anti-Aging Function. J Jpn Cosmet Sci Soc 2007;31:411~431, with permission.



**Fig. 2.** Photographs of wrinkle improvement. Left periorbital wrinkles before (wrinkle score 4.50) (A) and at 12 weeks after (wrinkle score 3.25) (B) intense pulsed light therapy. Right periorbital wrinkles before (wrinkle score 2.75) (C) and at 12 weeks after (wrinkle score 2.00) (D) 0.1% tretinoin cream application. The other participant of left periorbital wrinkles before (3.00) (E) and at 12 weeks after (wrinkle score 1.50) (F) erbium-doped yttrium aluminum garnet laser treatment. Right periorbital wrinkles before (wrinkle score 2.75) (G) and at 12 weeks after (wrinkle score 2.50) (H) 0.1% tretinoin cream application. Lt.: left, Rt.: right.

tion, peeling, and pruritus, but the severity was mild (visual analog scale [VAS] score,  $1\sim3$ ) and all of the symptoms decreased before the end of therapy without

specific treatment. In all participants, initial reactions to IPL therapy consisted of erythema, edema, and burning sensation at the treated area which was subsided within 2

days. In all participants who underwent fractional Er:YAG laser, initial reactions were erythema, edema, and pinpoint bleeding which was gradually disappeared within 1 week. One participant reported severe pain during fractional Er:YAG laser and withdrew after the second treatment. Average VAS scores for participants' satisfaction with fractional Er:YAG laser treatment, IPL therapy, and tretinoin cream were  $6.29\pm3.14$ ,  $5.20\pm3.04$ , and  $7.53\pm$ 2.42, respectively. And 11 of 19 participants chose the tretinoin cream treatment on a simple question "Which of the side would you undergo again or recommend to others?" of the final satisfaction survey. Although there was no significant difference among the 3 modalities, there was a preference for tretinoin cream, which is a minimally invasive and convenient treatment modality. The three treatment modalities used in this study were considered a favorable treatment in previous studies. Since the first study reported by Kligman et al.3, tretinoin has been shown in many clinical trials to be safe and effective for the treatment of photodamaged skin. It is known that the external application of tretinoin promotes the deposition of mucopolysaccharides in the epidermal keratinocytes and in the cornified layer, thus accelerating the production of collagen in the dermis. Thereby, tretinoin restores the decreased quantity of collagen in photoaged skin<sup>2</sup>. Goldberg and Cutler<sup>4</sup> studied 30 patients with periorbital, perioral, and forehead rhytides who were treated with IPL 1 to 4 times at 14-day intervals using a 645-nm filter with a cut-off of 40 to 50 J/cm<sup>2</sup>. Assessment by 2 independent observers showed "some" or "substantial" improvement in 83.3% of patients. The mechanism of action of IPL and nonablative or ablative laser application in skin rejuvenation is thought to be dermal remodeling which occurs through increased collagen I and type III deposition and collagen reorganization into parallel arrays of compact fibrils<sup>4,5</sup>. Recently, fractional photothermolysis (FP) has been introduced as a way to overcome the limitations of traditional ablative resurfacing<sup>6</sup>, and ablative FP using a 2,940-nm Er:YAG laser has become commercially available. This modality is as effective as traditional ablative approaches, but recovery time is considerably shortened and traditional postresurfacing sequelae are absent<sup>7</sup>. Lee et al.<sup>8</sup> reported that a fractional 2,940-nm short-pulsed Er:YAG laser is an effective and minimally invasive treatment modality for photodamaged skin in Asians. In comparison with previous studies, our study has several limitations such as the small sample size, short term follow-up and

lack of objective data evaluating wrinkle depth, such as profilometry and biopsy specimens. Nevertheless, it is that interesting that our study compared the use of a non-ablative nonlaser device, a fractional laser, and a topical agent, all of which have different levels of invasiveness and mechanisms of action. And also, in this study, mean baseline wrinkle score of all participants was 2.30, which was relatively shallow than previous studies. So, we could demonstrate that shallow periorbital wrinkles can be well responsive to topical tretinoin application, and that there was not much difference between IPL therapy and fractional Er:YAG laser treatment. In conclusion, we suggest that 0.1% tretinoin cream which is minimally invasive and convenient, can be an effective and safe treatment modality for fine periorbital wrinkles.

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