ORIGINAL ARTICLE

Clinical Improvement of Striae Distensae in Korean Patients Using a Combination of Fractionated Microneedle Radiofrequency and Fractional Carbon Dioxide Laser

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BACKGROUND Striae distensae are dermal scars with flattening and atrophy of the epidermis.

OBJECTIVE To evaluate the efficacy and safety of combination therapy with fractionated microneedle radiofrequency (RF) and fractional carbon dioxide (CO_2) laser in the treatment of striae distensae.

MATERIALS AND METHODS Thirty patients (30 female; mean age 33, range 21–51, Fitzpatrick skin type IV) with moderate to severe striae distensae were enrolled in this study. Patients were divided into three groups: fractional CO_2 laser only (n = 10), microneedle RF only (n = 10), and combination (n = 10).

RESULTS Improvement was evaluated using a visual analogue scale (range 1–4). Mean clinical improvement score of the dermatologist was 2.2 in the fractional CO_2 laser–treated group, 1.8 in the microneedle RF–treated group, and 3.4 in the combination group. Through skin biopsy, we observed thickened epidermis and a clear increase in the number of collagen fibers in the microneedle RF– and fractional CO_2 combination–treated sites. Consistent with these results, greater expression of transforming growth factor-β1 and stratifin was observed in treated sites.

CONCLUSION Combination therapy of fractionated microneedle RF and fractional CO_2 laser is a safe treatment protocol with a positive therapeutic effect on striae distensae.

The authors have indicated no significant interest with commercial supporters.

Striae distensae is an undesirable cutaneous disorder that can be divided into striae rubra, erythematous striae, and striae alba, as it matures and that may cause significant cosmetic problems.[1] Upon histologic examination, striae distensae is characterized by thinning and flattening of the epidermis with attenuation of rete ridges, a normal or small number of melanocytes, and thinning and retraction of dermal collagen and elastin.[1–4] It has been suggested that several factors contribute to striae distensae formation, such as mechanical stretching, normal growth, high serum levels of steroid hormones, and obesity.

Currently, fractional photothermolysis or 585-nm dye laser combined with radiofrequency (RF) appears to be a treatment option for striae distensa,[5,6] but with still unsatisfactory results, so that a new treatment method for striae distensae is in demand. A microneedle RF device has recently been introduced to treat various dermatologic indications, including wrinkles, atrophic scars, hypertrophic scars, and keloids.[7,8] The mechanism of its action is thought to be related to the fact that water, collagen, melanin, and the dermal microvasculature can absorb energy from the device, producing a bulk heating effect on the dermis that in turn induces growth factor

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secretion such as VEGF, FGF, resulting in dermal remodeling, but to the best of our knowledge, there has been no report describing the use of a microneedle RF device for the treatment of striae distensae alone, or combination therapy with fractional CO_2 laser. Therefore, this study was conducted to evaluate the clinical efficacy of combination treatment using fractionated microneedle RF and fractional CO_2 laser for the treatment of striae distensae.

Subject and Methods

Participants

The Institutional Review of Board of Keimyung University School of Medicine approved this clinical study. Thirty patients (30 female; mean age 33, range 21–51; Fitzpatrick skin type IV) with moderate to severe striae distensae on the abdomen, hips, or calves were enrolled. Patients were excluded from the study if they had recently received systemic steroids or had previously been treated with any other modalities such as topical retinoids, 1,450-nm diode laser, 595-nm pulsed dye laser (PDL), intense pulsed light photodynamic therapy, nonablative erbium glass fractional laser, or ablative 10,600-nm CO_2 fractional laser before. Patients with a high probability of becoming pregnant or a propensity for keloids or immunosuppression were also excluded.

Laser Treatment

Patients were divided into three groups: fractional CO_2 laser (CICU2; ilooda, Suwon, South Korea) only (n = 10), microneedle RF (Secret; ilooda) only (n = 10), and both (n = 10). Each group underwent three treatment sessions at 1-month intervals. A topical eutectic mixture of 2.5% lidocaine hydrochloric acid and 2.5% prilocaine (EMLA; AstraZeneca, Södertälje, Sweden) was applied to the entire striae under occlusion 30 minutes before therapy. The treatment settings were 1.5- to 3-mm microneedle penetrating depth, 4 to 7 intensity, and 70- to 130-ms RF conduct time in RF and 700 to 1,000 mJ and 0.7-mm density in fractional CO_2 laser. All treatments were applied over the entire striae for one pass. The use of a moisturizer several times daily for a few days after each treatment session was recommended to promote wound healing and prevent dryness. Patients were also instructed to avoid the use of any systemic or topical retinoids during the course of treatment. Photographs were taken using identical camera settings, lighting, and patient positioning at baseline and 1 month after the last treatment.

Objective and Subjective Evaluations

Two dermatologists performed objective clinical assessments in a blinded fashion by comparing before-and-after photographs in nonchronological order using a global improvement scale (grade 1, 0–30% = minimal improvement or steady state; grade 2, 30–50% = moderate improvement; grade 3, 51–80% = marked improvement; and grade 4, ≥81% = near total improvement). Investigators assessed and recorded possible side effects, including bleeding, pain, pruritus, scaling, crusting, erythema, and postinflammatory hyperpigmentation (PIH) at each visit (at 1-month intervals). Six months after the final treatment, the reported side effects were reassessed and analyzed. Two patients in the combination group were treated on the right side only so that histological comparison on treated and non-treated lesion could be obtained. Specimens were stained using hematoxylin and eosin, Masson-trichrome, and immunohistochemical staining using transforming growth factor beta 1 (TGF-β1), and stratifin antibodies (Santa Cruz Co., Santa Cruz, CA).

Results

Family history of striae distensae was observed in 70% of the participant population (n = 21). The following causes of striae distensae were observed: weight gain (n = 20), pregnancy (n = 6), and growth spurt (n = 4). The mean duration of striae distensae was 12.4 years (range 3–30 years).

A dermatologist evaluated improvement scores 6 months after the final treatment. Worsening of

striae was not observed in any patient. The mean clinical improvement score from the dermatologist was 2.4 in the fractional CO_2 laser–treated group, 2.0 in the microneedle RF–treated group, and 3.4 in the combination group. Similarly, the mean score from patients was 2.3 in the fractional CO_2 group, 1.9 in the microneedle RF group, and 3.6 in the combination group. In the combination group, four of 10 participants had grade 4 clinical improvement (Figure 1), and six of 10 participants had grade 3 clinical improvement (Figure 2). Three of 10 participants had transient PIH (Figure 3). A patient who had extensive striae distensae on the abdomen was treated in four sessions of combined therapy and showed marked improvement, compared with two treatment sessions (Figure 4). The results are summarized in Table 1.

Epidermal thickening and increased numbers of collagen bundles were observed in the treated sites on skin biopsy (Figure 5A). Masson-trichrome staining clearly showed large numbers of thick collagen fibers

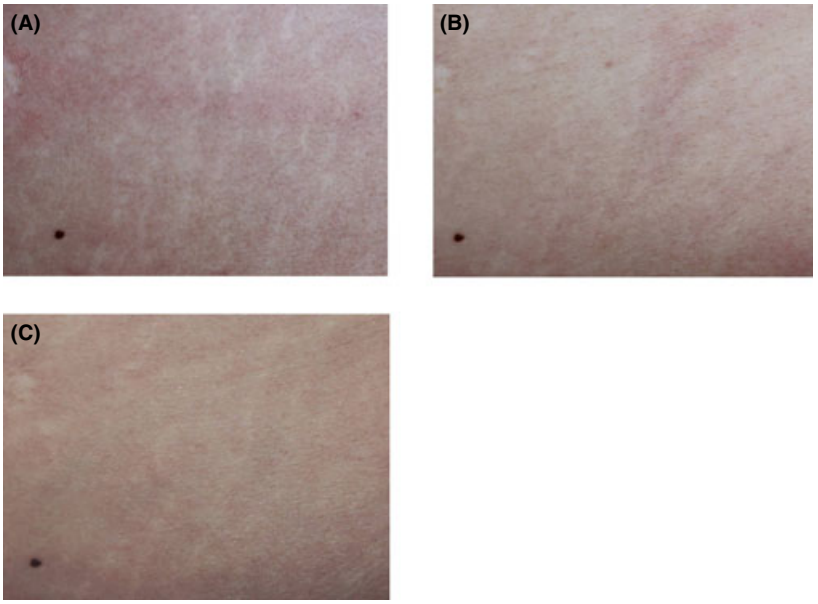

Figure 1. Striae distensae on the buttock before (A) and 3 (B) and 6 (C) months after three sessions of microneedle radiofrequency treatment with fractional carbon dioxide laser. The clinical improvement of striae distensae was grade 4.

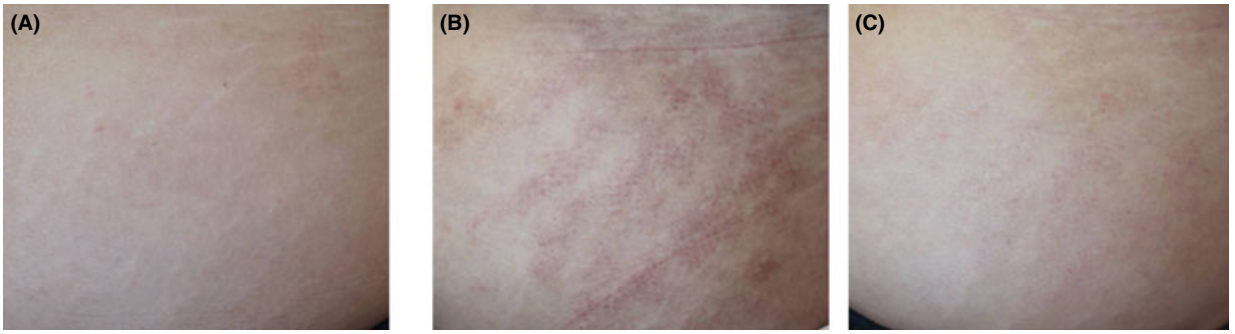

Figure 2. Striae distensae on the calf before (A) and 2 (B) and 6 (C) months after three sessions of microneedle radiofrequency treatment with fractional carbon dioxide laser. Clinical improvement of striae distensae was grade 3. Note the decreased width and blurred striae margin.

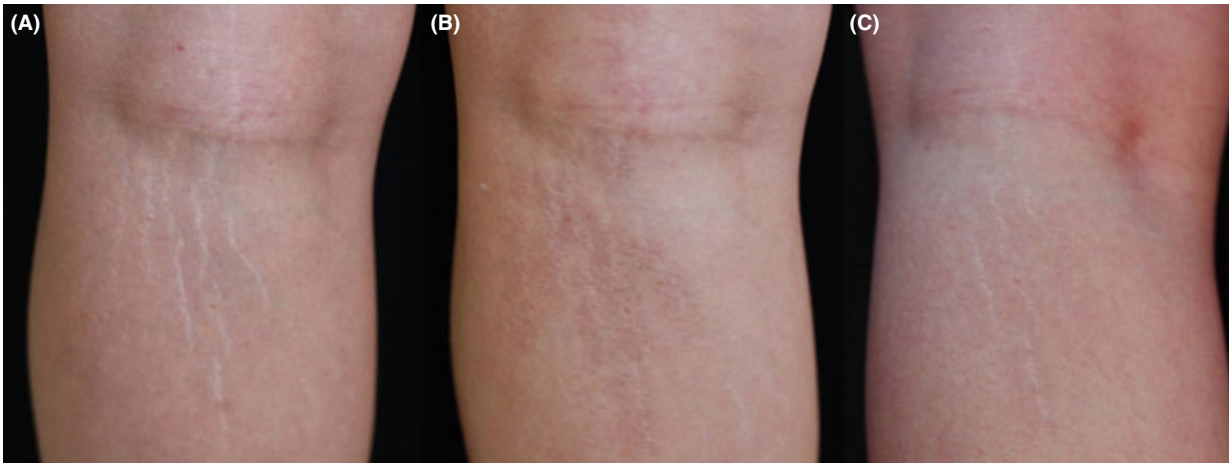

Figure 3. Striae distensae on the calf before (A) and 2 (B) and 6 (C) months after three sessions of microneedle radiofrequency treatment with fractional carbon dioxide laser. The clinical improvement of striae distensae was grade 3. Note the decreased width and blurred striae margin with transient postinflammatory hyperpigmentation.

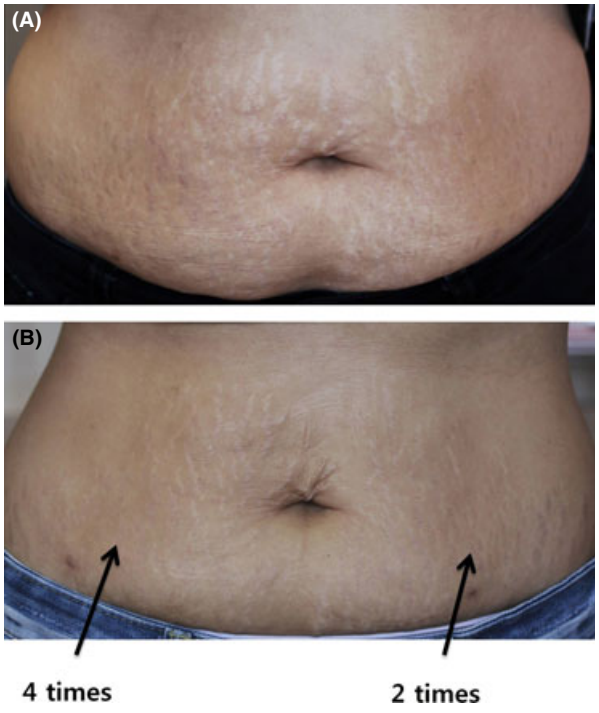

Figure 4. Striae distensae on the lower abdomen before (A) and 3 months after (B) final treatment sessions of microneedle radiofrequency and fractional carbon dioxide laser treatment. The right side of the abdomen was treated four times and the left side two times. Clinical improvement of striae distensae depended on the number treatment sessions.

in the combination treated sites (Figure 5B). Consistent with these data, high expression levels of TGF-β1 in the epidermis and dermis were observed in the treated sites (Figure 6A). Furthermore, high expression of stratifin, which plays an important role in epidermal and mesenchymal interaction during dermal remodeling, was observed in treated striae distensae tissues (Figure 6B). Transient PIH, pain, and pruritus occurred in all of the treatment groups but most commonly in the combination group. Of these side effects, PIH developed in 30% of patients in the combination group and improved spontaneously in 2 months. The other side effects were observed in 20% of patients in the combination group.

Discussion

Striae distensae is difficult to prevent or predict and can cause significant cosmetic problems. The histology of striae distensae is similar to that of scars, but the lesion matures from striae rubra to striae alba in several steps similar to those of the wound repair mechanism from wounding to scar formation.[2–4,9,10] In early lesion development, the so-called striae rubra, there is deep and superficial perivascular lymphocytic infiltration; inflammation resolves with time, but collagen bundles in the reticular dermis stretch parallel to the skin, resulting in flattening of the epidermis and elongation of rete ridges, followed by loss of collagen and elastic fibers in the substructures. There are several theories as to

TABLE 1. Baseline Patient Characteristics and Clinical Outcomes after Laser Treatment

Patient Number	*Age*	*Site*	*Treatment Type*	*Family Hx*	*Mechanism*	*Duration (year)*	*Type*	*Improvement Grade (VAS)*	*Patient Satifaction Grade (VAS)*	*Adverse Effects*
1	30	Abdomen	RF + FRX	Y	Pregnancy	3	A	3	2	–
2	30	Hip	RF + FRX	N	Growth spurt	20	A	3	4	–
3	30	Abdomen	RF + FRX	Y	Weight gain	12	A	3	4	Pruritus
4	34	Abdomen	RF + FRX	Y	Pregnancy	4	A/R	4	4	Pain
5	29	Abdomen	RF + FRX	Y	Weight gain	9	A	4	4	PIH
6	34	Calves	RF + FRX	Y	Weight gain	15	A	3	3	–
7	28	Abdomen	RF + FRX	N	Weight gain	8	R	4	4	PIH
8	28	Abdomen	RF + FRX	Y	Weight gain	8	A	3	3	PIH
9	26	Calves	RF + FRX	Y	Weight gain	10	A	3	4	–
10	32	Calves	RF + FRX	Y	Growth spurt	15	A	4	4	–
11	32	Calves	FRX	Y	Weight gain	20	A	4	4	PIH
12	29	Calves, buttock	FRX	N	Weight gain	12	A	2	3	–
13	34	Abdomen	FRX	Y	Pregnancy	5	A	2	2	PIH
14	37	Calves	FRX	N	Weight gain	20	A	2	2	–
15	24	Buttock	FRX	N	Weight gain	10	A	2	2	–
16	36	Calves	FRX	Y	Weight gain	10	A	2	2	–
17	30	Abdomen	FRX	Y	Weight gain	10	A	3	2	–
18	32	Abdomen	FRX	Y	Weight gain	15	A	2	2	Pruritus
19	40	Calves	FRX	Y	Growth spurt	15	A	3	2	–
20	41	Abdomen	FRX	Y	Pregnancy	10	A	2	3	–
21	51	Calves	RF	N	Weight gain	30	A	2	2	PIH
22	39	Calves	RF	Y	Weight gain	10	A	2	1	–
23	40	Calves	RF	N	Weight gain	20	A	1	2	–
24	21	Calves	RF	Y	Weight gain	10	A	2	3	PIH
25	41	Abdomen	RF	N	Pregnancy	10	A/R	2	2	Pruritus
26	31	Calves	RF	N	Weight gain	15	A	3	2	–
27	45	Calves	RF	Y	Weight gain	30	A	2	2	–
28	30	Buttock	RF	Y	Weight gain	10	A	2	2	Pain
29	27	Calves	RF	Y	Growth spurt	10	A	2	1	–
30	29	Abdomen	RF	Y	Pregnancy	5	R	2	2	–

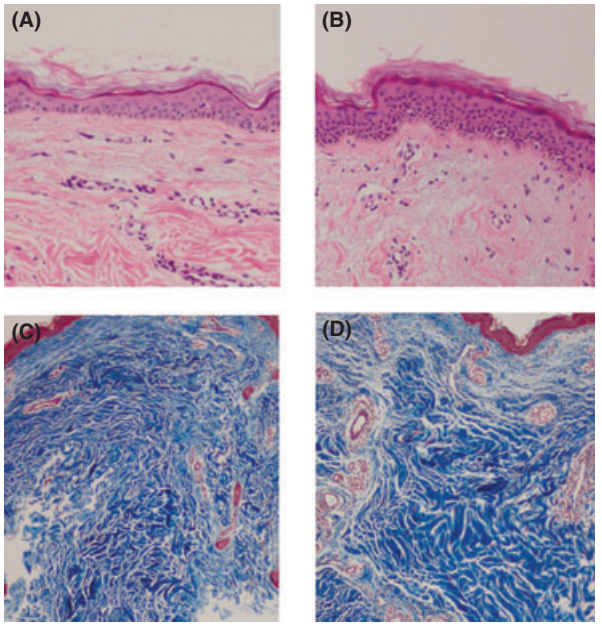

Figure 5. Dermal remodeling and neocollagenesis after microneedle radiofrequency and fractional CO_2 laser treatment. Note the thickened epidermis (B) and greater numbers of and thicker collagen bundles in the dermis (D) than at baseline (A, C, respectively). (A, B, hematoxylin and eosin ×100; C, D, Masson trichrome stain ×40).

how striae distensae develop, including rupture of the connective tissue framework through mechanical stretch by pregnancy, obesity, or normal growth spurts; increased catabolic effect of fibroblasts because of steroid hormones; and specific infections that excrete stria toxin.[11–13]

There have been numerous challenges, but still there is no criterion standard or established protocol in the treatment of striae distensae. As simple topical applications, tretinoin, hydrating creams, topical oil, and several acid agents were tried but were not satisfactory.[14] Several laser treatments and light source devices have been tried, including intense pulsed light, PDL, long-pulse neodymium-doped yttrium aluminum garnet laser, ablative fractional or conventional CO_2 laser, and nonablative erbium glass fractional laser.[3,4,6,15–17]

Laser therapy has recently become the mainstay of treatment for striae distensae. The 585-nm PDL has been used most frequently for the treatment of striae

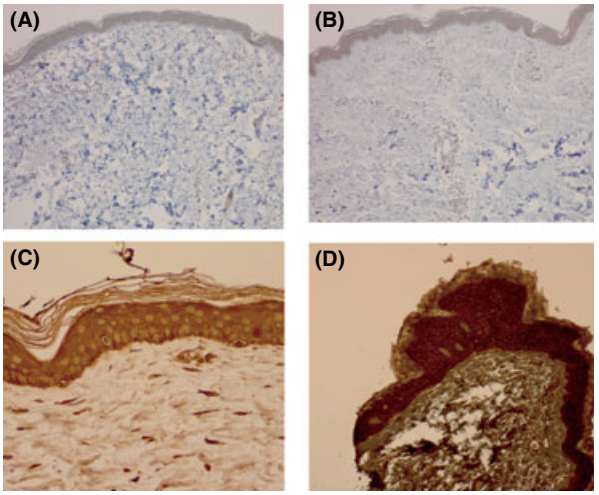

Figure 6. Higher expression of transforming growth factor beta 1 (TGF-β1) and stratifin after microneedle radiofrequency with fractional carbon dioxide laser treatment. Note the higher expression of TGF-β1 (B) and stratifin (D) in the thickened epidermis and dermis according to immunohistochemistry than at baseline (A, C, respectively). (A, B, ×100; C, D, ×200).

distensa,[6,18] and trials of combination RF therapy with 585-nm PDL have produced favorable outcomes with minimal side effects, but a new treatment method is needed to improve treatment of striae distensae.

A fractionated microneedle RF device has been introduced with the purpose of skin rejuvenation.[7,8] Fractionated microneedle RF can deliver higher volumetric heating and deeper heat diffusion than PDL such that we can expect more-effective dermal remodeling. Furthermore, skin needling with microneedles has been reported to stimulate migration and proliferation of keratinocytes and fibroblasts by inducing the release of several growth factors.[8,19] Even though there have been several trials of application of fractionated microneedle RF device to acne scars, there are no reports on the application of the device in striae distensae. Therefore, in this study, we investigated the clinical efficacy of and histologic changes after fractionated microneedle RF combined with fractional CO_2 laser by extending its use from skin resurfacing and rejuvenation to striae distensae.

Our data showed that fractionated microneedle RF combined with fractional CO_2 laser induced clinical

improvement of striae distensae without serious side effects. This is, to our knowledge, the first study using combined therapy of microneedle fractional RF with fractional CO_2 laser that showed statistically significant improvement in roughness and thinning of the skin. Subjects who received combined treatment showed clinical improvement in skin texture and width according to investigator assessment, which was mean graded 3. 4. In particular, combination treatment markedly increased the number and thickness of collagen fibers. Greater expression of TGF-β1 and stratifin is likely to be responsible for accumulation and thickening of collagen fibers in the dermis. Stratifin, which is a novel keratinocyte-derived extracellular matrix modulating factor for dermal fibroblasts, induces matrix metalloproteinase-1 expression and activity in dermal fibroblasts to cause dermal remodeling.[20]

Side effects were also analyzed in this study. PIH was the only notable problem, but it spontaneously resolved in 2 months. All of the side effects, including pain and pruritus, were more frequently detected in the combination group, but all side effects were acceptable and temporary.

In conclusion, fractionated microneedle RF treatment could be an effective treatment for striae distensae, and combination treatment with fractionated CO_2 laser could be a better choice without significant adverse effects.

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