ORIGINAL CONTRIBUTION

Combination Tripeptide/Hexapeptide Serum with 1540 nm Nonablative Fractional Laser for the Treatment of Striae Distensae: A Pilot Study

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ABSTRACT

Striae distensae (SD) are associated with negative psychosocial effects. Improvements have been shown with non-ablative fractional lasers (NAFL). Topical peptides have also been effective in cutaneous rejuvenation; however, no studies have examined combination therapy for striae. Our study evaluated the efficacy and safety of a peri-procedural tripeptide/hexapeptide serum as an adjunct to 1540 nm NAFL for the treatment of SD in 10 patients. All patients reported subjective improvement. The addition of tripeptide/hexapeptide serum increased the objective improvement, reduced the incidence of post-inflammatory hyperpigmentation, and increased patient satisfaction. (*SKINmed*. 2020;18:337–341)

Striae distensae (SD), often referred to as stretch marks, typically occur from stretching of the skin, which causes aberration of dermal collagen and elastic fibers. The majority of SD occur during pregnancy and pubertal growth, while other causes include rapid weight gain or loss.[1] Frequently, SD initially appear as linear erythematous to violaceous plaques, termed striae rubra (SR). They then become hypopigmented and depressed due to epidermal atrophy and are then referred to as striae alba (SA).[2]

Despite frequent occurrence, there is no consistently effective therapy.[1] While not physically harmful, the psychosocial implications are often significant. SA, which are considered to be end-stage, are considerably more resistant to treatment. Therapies have focused on resurfacing as well as reorganizing aberrant dermal collagen and elastin. There are limited data supporting the use of topical therapies, including retinoids, chemical peels, silicone gel, and hyaluronic acid.[1] The irritation and burning that can be associated with retinoids and chemical peels, in addition to the underwhelming patient satisfaction and clinical improvement, often make these treatments undesirable. There are several small case series demonstrating improvement with microneedling, especially when combined with platelet-rich plasma and/or chemical peels.[1]

More recently, laser surgery has shown promise. Although ablative lasers have offered clinical improvement of SD, treatment has been limited due to downtime and risk for post-inflammatory hyperpigmentation (PIH), especially in skin of color.[3] In contrast, non-ablative fractional lasers (NAFL) have been shown to offer nearly comparable results, but with less downtime and PIH.[3,4] Overall, many regard NAFL as the first-line treatment.

We have previously established the safety and efficacy of the 1540 nm NAFL (Cynosure ICON, Cynosure Inc., Westford MA) in a split-abdomen study of SD.[4] This study examines the safety and efficacy of an added peri-procedural tripeptide/hexapeptide serum (TriHex Technology, Alastin Skincare Inc., Carlsbad, CA), which has previously been shown on histopathologic examination to increase collagen and elastin.[5] Clinically, the tripeptide/hexapeptide serum has been demonstrated to decrease dyspigmentation, downtime, and erythema associated with NAFL. We hypothesize that the addition of tripeptide/hexapeptide serum as an adjunct to the 1540 nm NAFL would reduce the post-procedural downtime, improve the outcome, and reduce the incidence of PIH.

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MATERIALS AND METHODS

In this Institutional Review Board (IRB)-approved pilot study, 10 patients aged between 18 and 60 years with abdominal SD were enrolled. Exclusion criteria included pregnant and/or lactating women; those with known allergy to the topical agent; use of oral corticosteroids and oral retinoids within the past 2 months and 12 months, respectively; preexisting dermatologic conditions in the area; infections or abnormal scarring; and SD having undergone topical, laser, or surgical treatments within the past 12 months.

Patients were instructed to apply the tripeptide/hexapeptide serum twice daily starting 2 weeks prior to their first laser treatment. Laser treatments were completed at 2–4-week intervals. A final follow-up visit was conducted at 90 days following the final treatment. The initial visit comprised of investigator and subject assessments. After laser treatment, subjects were instructed to apply a thin layer of the tripeptide/hexapeptide serum twice daily to the treatment area until the final follow-up visit. Patients were instructed to practice strict photoprotection and apply broad spectrum sunscreen (SPF 30) daily to the treatment area.

During treatment visits, topical lidocaine 30% ointment was applied under occlusion for 60 minutes prior to treatment. The 1540 nm NAFL with the XD microlens handpiece and the XF microlens handpiece (Cynosure ICON, Cynosure Inc., Westford, MA) were utilized, with two passes for each handpiece. Both were at settings of 15 ms pulse duration and 50 J/cm^2 fluence for a total 25% density. If significant PIH developed, patients were treated with hydroquinone 4% cream twice daily in addition to the tripeptide/hexapeptide serum.

At each treatment visit and at the follow-up visit, subjects and investigators reported the global aesthetic improvement of SD. After each laser treatment, subjects rated their level of pain during the procedure (1 = no pain; 10 = severe pain). At the follow-up visit, subject satisfaction was determined by the Likert rating of various statements. Subjects also reported their percent overall improvement.

Punch biopsies of representative SD were performed on a randomly chosen patient. The first biopsy was performed at the initial visit prior to treatment, and the second biopsy was performed at the follow-up visit. The sites for the biopsies were within the same representative SD to allow for accurate histologic comparison. The post-treatment biopsy was performed at least 2 cm from the site of pre-treatment biopsy to prevent sampling scar tissue. Biopsy specimens were stained with hematoxylin and eosin (H&E) and also Verhoeff-Van Gieson (VVG) to evaluate elastic fibers. Histologic review was performed objectively using a previously established pathology scale[4] by an independent board-certified dermatopathologist.

All statistical analyses were performed independently. Paired *t*-test was used to compare the values of this study with our historic study of SD treatment using NAFL alone. Subjective improvement scores in the historic study were doubled to approximate scoring in this study. Using top-box score, extreme satisfaction was defined as scores of 8–10.

RESULTS

Subject Demographics

A total of nine patients completed the study, while one patient dropped out due to the inconvenience of travelling to the treatment site. The average patient age was 38 years (median, 36; min, 27; max, 57). Of all patients, 89% were women. Fitzpatrick skin types (FST) I-V were represented. All SD were SA, which had been present for an average of 12 years (median, 8; min, 0.75; max, 28). Patients received an average of five NAFL treatments (median, 6; min, 4; max, 6). Treatments were an average of 22 days apart (median, 20; min, 16; max, 33).

Improvement in Striae

Within the 2-week pretreatment period using the tripeptide/hexapeptide serum alone, 33% of patients demonstrated 10%–15% improvement in SD (Figure 1). At the final follow-up visit, there were improvements in skin tightness and texture in addition to reduction of erythema (Figure 2).

Histopathologic Analysis

Compared to the pretreatment biopsy, there was a notable increase in the density of collagen bundles in the post-treatment biopsy (Figure 3). Using a previously established pathology scale,[4] the increase was scored as 2 (26%–50% increase) by an independent, non-study dermatopathologist. With VVG staining, there was a score of 4 (76%–100% increase) for elastic fibers observed between the biopsies (Figure 4).

Patient and Provider Rating

Improvement was noted in patient satisfaction. At the last treatment, patients and providers rated SD improvement on a 6-point Likert scale (−3 = very much worse to +3 = very much improved). The average patient score was 2 (median, 2; min, 1; max, 3), while the average provider score was also 2 (median, 2; min, 2; max, 3). Patients who received six treatments compared to four treatments had similar improvement. Intra-procedural pain was rated an average of 4.6 out of 10, with 10 being the worst.

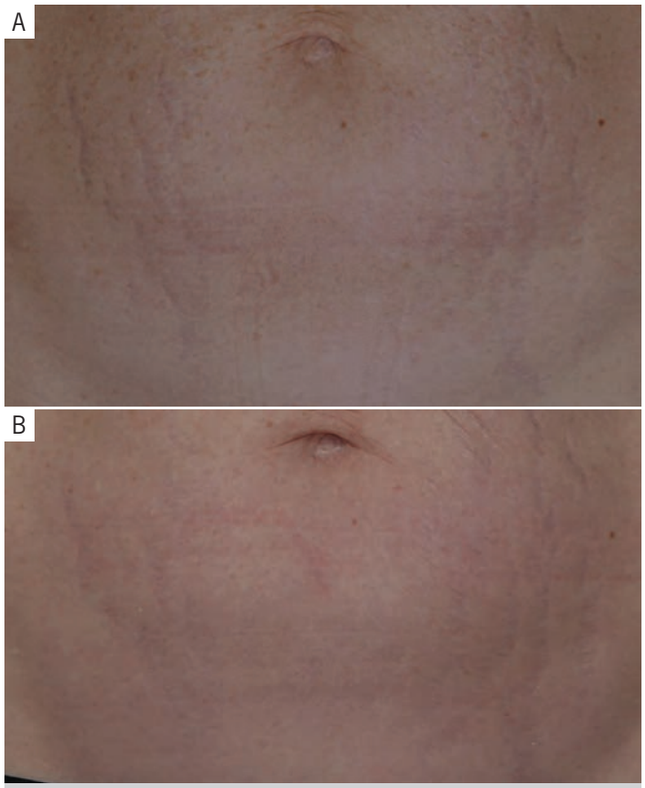

Figure 1. (A) SD prior to treatment. (B) SD after 2 weeks of treatment with tripeptide/hexapeptide serum alone prior to the initiation of laser treatment.

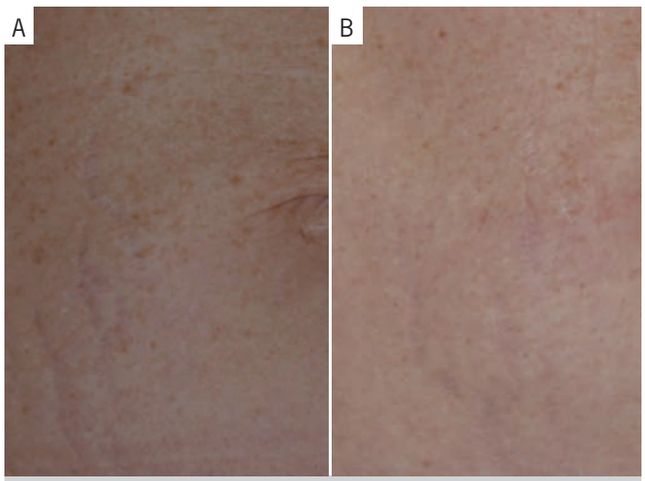

Figure 2. (A) SD prior to treatment. (B) SD at follow-up visit.

Adverse Effects

Adverse effects included post-procedural edema lasting a few hours and erythema lasting 1–3 days. Two patients with FST III and V had mild and moderate PIH, respectively. At the final follow-up visit, the mild PIH had resolved without bleaching agents, and the moderate PIH resolved using hydroquinone.

Comparison to Historic Study

In comparison to our previous study on the treatment of SD with NAFL alone, the mean subjective improvement scores between the studies were not significantly different ($P = 0.6003$) (Table 1); however, the mean objective improvement scores were significantly higher with the addition of tripeptide/hexapeptide serum ($P = 0.0070$) (Table 2). In the previous study with NAFL alone, PIH occurred in 100% of patients. With the addition of tripeptide/hexapeptide serum, only 33% of patients developed PIH ($P = 0.0090$). Interestingly, this significant decrease in PIH occurred even with the inclusion of darker skin types in this study. The mean satisfaction scores were higher in this study compared to the historic study (8.4 vs. 4.2; $P < 0.0001$) (Table 3). The percentage of extreme satisfaction was also higher for this study (78% vs. 0%; $P = 0.0023$).

DISCUSSION

Although SD are common, they remain challenging to treat despite the availability of several treatment modalities. In the past, topical treatments, including tretinoin, have yielded inconsistent and unsatisfying results.[6] Various lasers and light devices have also been studied, including pulsed dye laser and intense pulsed light, but have been found to be more effective in SR. SR display more acute histopathologic changes and can therefore be more responsive to therapy. In contrast, SA have more chronic changes and are typically more resistant to treatment. In this study, all patients had SA.

Ablative and NAFL are the most commonly used lasers to treat SD.[3,7–9] The fractional 1540 nm laser has been frequently studied. This laser creates narrow zones of thermal injury, while leaving the stratum corneum intact. The unaffected tissue between the thermal zones serves as a reservoir for healing. With less post-procedural downtime and fewer adverse effects, NAFL tends to be better tolerated than their ablative counterparts.

This is the first study to combine a peri-procedural tripeptide/hexapeptide serum with laser therapy for the treatment of SD. In a randomized split face/décolleté trial, the addition of tripeptide/hexapeptide serum prior to and following NAFL treatment resulted in reduced healing time, increased reduction of lentigines, greater textural improvement, and higher global skin quality scores compared to NAFL alone.[10] Another study in those with mild-to-moderate rhytides and skin laxity showed that treatment with tripeptide/hexapeptide serum for 12 weeks was associated with histologic increases in collagen and elastin in 100% and 60%

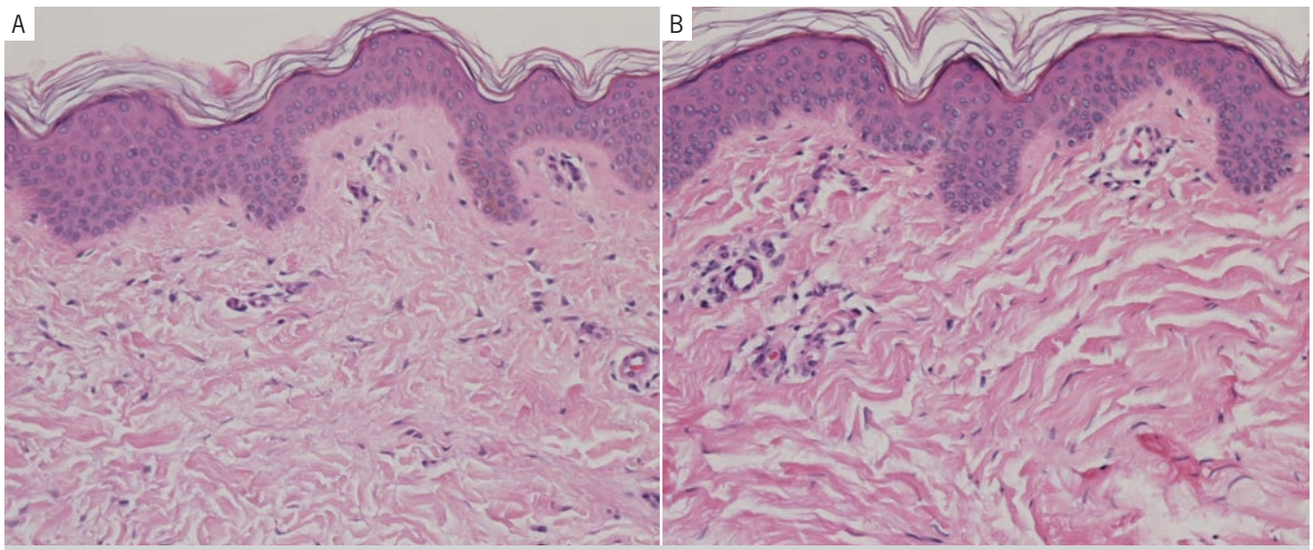

Figure 3. (A) Skin biopsy prior to treatment (H&E, 200× magnification). (B) Skin biopsy at follow-up visit showing increased collagen bundles (H&E, 200× magnification).

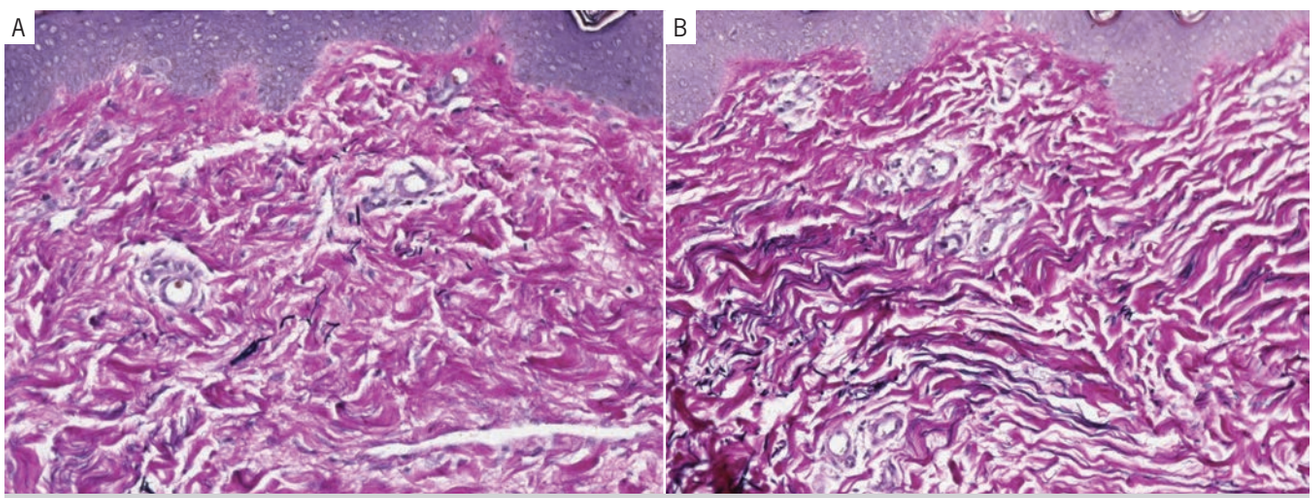

Figure 4. (A) Skin biopsy prior to treatment (VVG, 200× magnification). (B) Skin biopsy at follow-up visit showing increased elastic fibers (VVG, 200× magnification).

Table 1. Comparison of Subjective Improvement Scores between Treatments

Treatment	Mean Score	SD	95% CI	
NAFL	2.3	0.7	1.8	2.9
NAFL + TriHex	2.2	0.6	1.7	2.6
P-value	0.6003	0.7	-0.5	0.8

Abbreviations: CI, confidence interval; NAFL, non-ablative fractional lasers; SD, standard deviation.

Table 2. Comparison of Objective Improvement Scores between Treatments

Treatment	Mean Score	SD	95% CI	
NAFL	1.5	0.7	1.0	2.1
NAFL + TriHex	2.4	0.5	2.1	2.8
P-value	0.0070			

Abbreviations: CI, confidence interval; NAFL, non-ablative fractional lasers; SD, standard deviation.

Table 3. Comparison of Patient Satisfaction Scores between Treatments

Treatment	Mean Score	SD	95% CI	
NAFL	4.2	1.2	3.3	5.1
NAFL + TriHex	8.4	1.7	7.2	9.7
P-value	<0.0001			

Abbreviations: CI, confidence interval; NAFL, non-ablative fractional lasers; SD, standard deviation.

of patients, respectively.[5] The peptides in the serum are matrikines, which can promote the clearance of unwanted protein fragments by increasing matrix metalloproteinase (MMP) production, reduce the oxidative stress, reduce the MMP-1 destruction of normal collagen fragments, promote the optimal function of fibroblasts, and improve the function of the proteasome system. The effects of the tripeptide/hexapeptide serum make it an ideal treatment for scars, as well as SD.[11]

A major limitation of this study is that it was a pilot study with a small sample size. There was also no concurrent control; however, a historic control completed at the same institution was used in its place. SD are often hard to capture accurately on photography, and their improvement can be even more challenging to measure, which is why both sides were treated with NAFL and tripeptide/hexapeptide serum. Biopsies were originally intended to be completed in two patients; however, the second patient never returned for a follow-up biopsy. In a pilot study with nine patients, biopsies in a single patient were considered to be representative.

CONCLUSIONS

Tripeptide/hexapeptide serum is a safe and effective adjunct to NAFL for the treatment of abdominal SD. All patients reported subjective improvement. The addition of tripeptide/hexapeptide serum increased the objective improvement, reduced the incidence of PIH, and increased patient satisfaction. Additional large-scale studies are necessary for a more thorough evaluation of the utility of tripeptide/hexapeptide serum as an adjunct to NAFL.

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DISCLOSURE

Nazanin Saedi is a consultant for Cynosure and Alastin. The remaining authors have no relevant conflicts of interest to declare.

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