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Tripeptide and hexapeptide topical as adjunct to nonablative fractional resurfacing for photodamage: A randomized split-face trial

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Abstract

Background: Topical adjuncts have been investigated to improve clinical outcomes associated with laser resurfacing for photodamage and cutaneous aging. One such product is a tripeptide/hexapeptide serum, which has been shown to increase dermal collagen and elastin as well as improve postprocedural recovery following treatments.

Aims: A randomized, blinded, split-face, comparative trial was performed to assess the utility of a tripeptide/hexapeptide serum as a peri-procedural adjunct to nonablative fractional laser resurfacing.

Patients/Methods: A total of 20 subjects were enrolled. Each hemiface was randomized to either tripeptide/hexapeptide serum or bland moisturizer for twice daily application starting 14 days prior to first laser treatment and continuing until 60 days after. All subjects received 2 treatments to entire face approximately 1 month apart with 1927 nm thulium nonablative fractional laser. Clinical measures and immediate postprocedural recovery were assessed.

Results: For each hemiface, scores improved for all measures, including global photodamage, lentigines, pores, radiance, texture, and tone at 30 and 60 days. The tripeptide/hexapeptide serum had greater improvements for all measures at both time points, except for radiance at 60 days, which was equal. In cases where clinical ratings differed between sides, tripeptide/hexapeptide serum more frequently had the superior outcome. Overall, subjects were satisfied with tripeptide/hexapeptide serum. No significant adverse events were observed.

Conclusion: Addition of tripeptide/hexapeptide serum as a peri-procedural adjunct to nonablative fractional laser resurfacing improved various clinical measures of photodamage and cutaneous aging and the immediate postprocedural recovery. The tripeptide/hexapeptide serum was demonstrated to be safe, well-tolerated, and well-liked by subjects.

KEYWORDS

aesthetics, dermatology, lasers, peptides, skin aging

1 | INTRODUCTION

Clinical signs of aging and photodamage are common complaints of many cosmetic patients. In combination with intrinsic aging, various environmental stressors are known to accelerate aging processes, including ultraviolet radiation, smoke, and pollution.[1] Over time, cellular damage can accumulate and cause harmful effects to normal cellular function, protein maturation, and physiologic processes.[2-6] Clinically, this can manifest as fine lines and wrinkles, textural irregularities, decreased elasticity, and dyspigmentation.

Since its introduction, nonablative fractional laser (NAFL) resurfacing has become popular for the treatment of photodamage and for cutaneous rejuvenation due its ability to achieve clinical results without prolonged downtime.[7,8] It also has an improved safety profile compared to its ablative counterpart. This technology allows thermal energy to be delivered to the dermis without detrimental epidermal damage. NAFL has been used to treat various skin disorders, including photodamage, dyspigmentation, acne scars, and striae.

Recently, the use of topical adjuncts has been investigated to improve the clinical outcomes and downtime associated with laser resurfacing. One such product is a tripeptide and hexapeptide (TriHex Technology, Alastin Skincare, Carlsbad, CA) serum, which has been used by several experts in the field of cosmetic dermatology.[9] This product can influence various cutaneous processes in order to increase collagen and elastin in the skin as well as improve postprocedural recovery following procedures.[10-15]

We hypothesize that the addition of TriHex serum as a peri-procedural adjunct to NAFL resurfacing for the treatment of facial photodamage and cutaneous aging can improve clinical outcomes and immediate postprocedural recovery. We performed a randomized, blinded, split-face, comparative trial to assess the utility of TriHex serum.

2 | MATERIALS AND METHODS

Twenty healthy subjects seeking treatment for facial photodamage and cutaneous aging were enrolled. Power calculations showed that 20 patients were sufficient. This was based on previous data and experience with the combination treatment. This study was approved by an independent IRB. Informed consent was obtained. Subjects were included if they were between 25-70 years old with no known medical conditions that would interfere with study participation; Fitzpatrick Skin Types II-IV; free of bruises, swelling, or dermatologic disorders that would interfere with study results or increase risk of adverse reaction; willing to avoid extended periods of sun exposure and artificial tanning during the study; and willing to refrain from receiving neurotoxin and filler injections or other energy-based device treatments during the study.

Subjects were excluded if they had active systemic infections or skin conditions that might alter wound healing; known allergy to lidocaine or other topical anesthetic; history of keloids or hypertrophic scars; treatment with systemic retinoid in the prior 6 months; systemic steroids, chemical peels, lasers, light-based devices, radiofrequency, or dermabrasion in the prior 3 months; microdermabrasion in the prior 1 month; alpha-hydroxy acids, salicylic acid, benzoyl peroxide, retinol, tretinoin, vitamin C, or vitamin E in the prior 14 days; and tanning or self-tanner use in the prior 7 days.

For all subjects, each hemiface was randomized to treatment with either Regenerating Skin Nectar with TriHex Technology (RSN) or bland moisturizer (Cetaphil lotion, Galderma Laboratories, Fort Worth, TX) for twice daily application starting 14 days prior to the first NAFL treatment and continuing until 60 days after. Randomization was completed via computerized random number generator. All subjects and investigators were blinded to which topical was assigned to each hemiface. All subjects received two treatments to the entire face approximately 1 month apart with the 1927 nm thulium NAFL (Fraxel Dual, Solta Medical, Hayward, CA). A gentle cleanser (Cetaphil cleanser, Galderma Laboratories, Fort Worth, TX) and broad-spectrum sunscreen (Neutrogena Ultrasheer, Johnson & Johnson, New Brunswick, NJ) were provided to all subjects to use during the study.

On the day of NAFL treatment, topical EMLA cream (lidocaine 2.5%/prilocaine 2.5%) was applied for 60 minutes and removed prior to treatment. Subjects received full-face treatment with the 1927 nm thulium NAFL (10 mJ fluence, 40%-65% density, 4-6 passes). Immediately following treatment, each topical was applied to the assigned hemiface. Subjects were evaluated during postprocedural recovery and at 30 and 60 days following the first treatment.

The VISIA photography system (Canfield Scientific, Fairfield, NJ) was utilized. Recovery was assessed for each hemiface using 4-point Likert scale (0 = none to 3 = severe) for various measures, including stinging, tenderness, dryness, and itching. Investigators also rated the subject's photodamage on each hemiface using 10-point Likert scale (0 = absent to 9 = severe) for global photodamage and various measures, including lentigines, pores, texture, tone, and radiance. Adverse events were also assessed. Statistical analysis was performed using paired and nonpaired *t*-test where appropriate.

3 | RESULTS

3.1 | Subject demographics

A total of 20 subjects completed the study. Mean age was 52 years (R: 39-69 years). Of all subjects, 95% (n = 19) were female. In terms of Fitzpatrick skin type, 85% of subjects were Type II (n = 17) and 15% (n = 3) were Type III.

3.2 | Investigator rating of clinical measures

For the bland moisturizer-treated side, scores significantly improved for all measures of lentigines (Δ-0.7, $P < .00001$; Δ-1.30, $P < .00001$), pores (Δ-1.10, $P = .00007$; Δ-1.80, $P = .00005$),

radiance (Δ-1.20, $P < .00001$; Δ-1.85, $P = .00004$), texture (Δ-1.10, $P = .00001$; Δ-1.80, $P = .00002$), and tone (Δ-1.00, $P < .00001$; Δ-1.70, $P = .00005$) at 30 and 60 days, respectively. For the RSN-treated side, all scores significantly improved for measures of lentigines (Δ-1.05, $P < .00001$; Δ-1.50, $P < .00001$), pores (Δ-1.20, $P = .00007$; Δ-1.90, $P = .00003$), radiance (Δ-1.30, $P < .00001$; Δ-1.85, $P < .00001$), texture (Δ-1.25, $P < .00001$; Δ-1.90, $P < .00001$), and tone (Δ-1.20, $P < .00001$; Δ-2.00, $P < .00001$) at 30 and 60 days, respectively. RSN had greater improvements for all measures at both time points, except for radiance at 60 days, which was equal (Figure 1). However, these trends were not statistically significant. In cases where the clinical ratings at both time points were different between each side, RSN more frequently had the superior outcome for all measures, which was significant for lentigines ($P = .0086$) and tone ($P = .0030$).

Global photodamage scores improved with use of bland moisturizer (Δ-1.10, $P < .00001$; Δ-1.90, $P < .00001$) and RSN (Δ-1.30, $P < .00001$; Δ-2.00, $P < .00001$) at 30 and 60 days, respectively. The degree of improvement was greater with RSN at both time points, which was greatest at 30 days ($P = .0421$) (Figure 1). In cases where the clinical ratings at both time points were different between each side, RSN more frequently had the superior outcome ($P = .0037$).

3.3 | Rating of immediate postprocedural recovery

Overall, the greatest increases in stinging and tenderness and decreases in dryness and itching occurred at post-treatment day 2. Mean subject ratings demonstrated that postprocedural stinging (Δ-1.58 vs Δ-1.48) and tenderness (Δ-0.73 vs Δ-0.65) decreased to a greater degree with RSN compared to bland moisturizer, while postprocedural dryness (Δ1.38 vs Δ1.43) and itching (Δ0.30 vs Δ0.33) increased to a lesser degree (Figure 2). However, these trends were not statistically significant.

3.4 | Satisfaction with product

Overall, subjects were satisfied with RSN. In total, 95% and 85% agreed that RSN felt good on the skin immediately after laser treatment at 30 and 60 days, respectively. This increased to 95% and 90% when describing all topical applications during the study period. At 60 days, 60% of subjects were more likely to consider having laser treatment again if RSN was included, and 75% would recommend RSN to others considering laser treatment.

3.5 | Safety

No significant adverse events were observed during the study. There were no reports of allergic or irritant contact dermatitis in either group.

4 | DISCUSSION

Clinical signs of aging can be the result of multiple factors, including inherent processes and outside influences, such as ultraviolet rays, smoking, and pollution. This is a common patient complaint experienced by cosmetic dermatologists, which also includes photodamage. Many treatment options are available to treat both, including chemical peels, intense pulsed light, laser resurfacing, microneedling, platelet-rich plasma, and radiofrequency.[16-22] The use of NAFL resurfacing for facial rejuvenation continues to be popular due to a desire for clinical efficacy without prolonged downtime. Its thermal columns of injury stimulate neocollagenesis and neoelastogenesis, which can ultimately improve clinical signs of aging. Treatment with NAFL is known to cause little-to-no downtime for most patients, and the associated edema and erythema are expected to resolve within days of treatment.

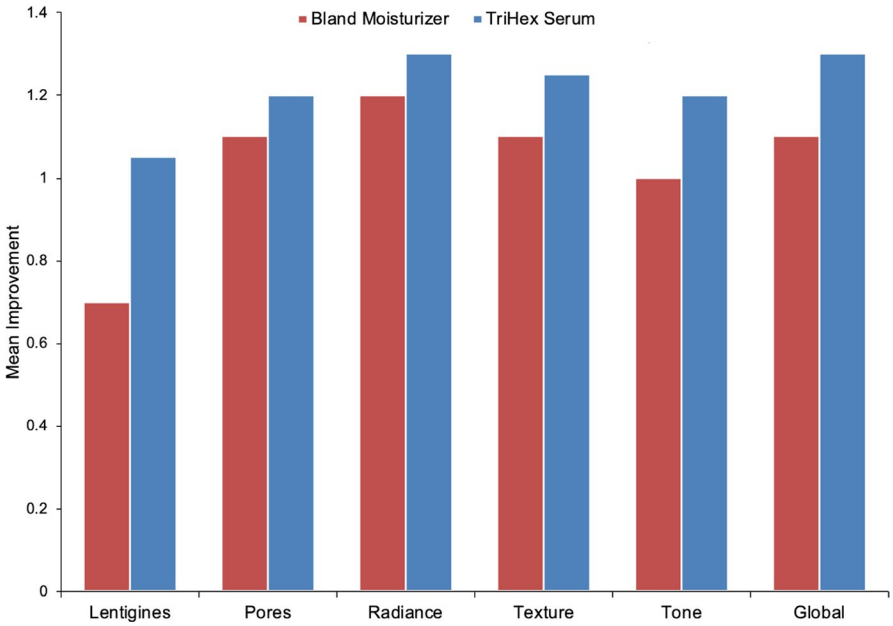

FIGURE 1 Improvement in mean investigator rating of various clinical measures from pretreatment to 30 d

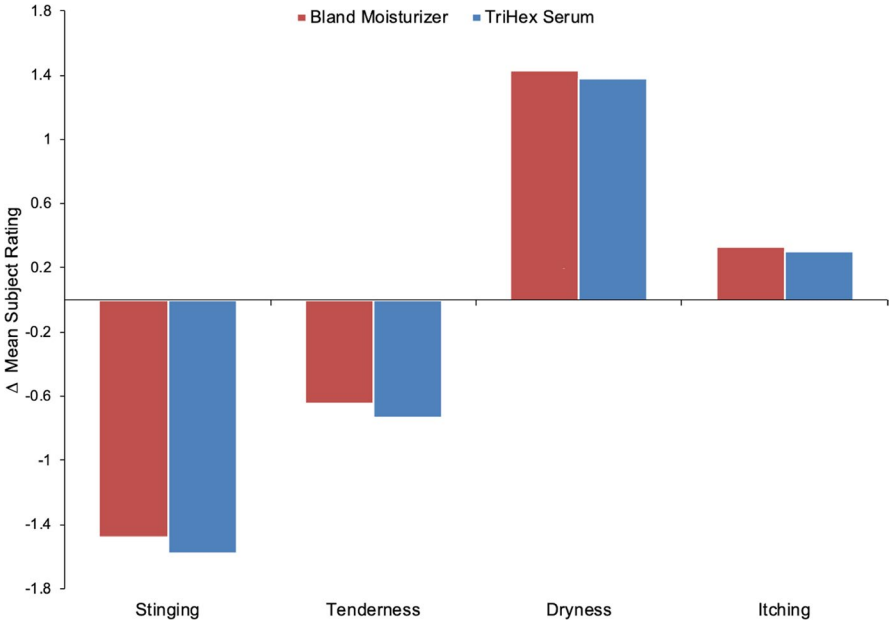

FIGURE 2 Changes in mean subject rating of various clinical measures from post-treatment to post-treatment day 2

FIGURE 3 Photographs of female subject using bland moisturizer on right hemiface (top row) and TriHex serum on left hemiface (bottom row) immediately following first treatment, on post-treatment day 2, and on post-treatment day 4 (from left to right)

The addition of TriHex serum to resurfacing procedures has been evaluated. Preprocedural preparation of the extracellular matrix (ECM) can optimize wound healing responses. TriHex serum contains matrikines, which are ECM protein fragments that can influence the ECM. Matrikines can improve the clearance of unwanted protein fragments, decrease oxidative stress, promote optimal fibroblast function, and reduce undesirable damage to normal collagen fragments.[10-12] In addition to increasing dermal collagen and elastin, TriHex serum has also been demonstrated to improve postprocedural recovery following laser treatments.[13-15] A recent randomized, split-face trial of 10 subjects compared the peri-procedural use of a topical regimen including TriHex serum to a basic regimen following NAFL treatment of the face and neck.[23] TriHex serum was associated with reduced healing time, greater textural improvement, improved reduction of lentigines, and superior global skin quality scores. Participants also reported subjective improvements in the look and feel of their skin.

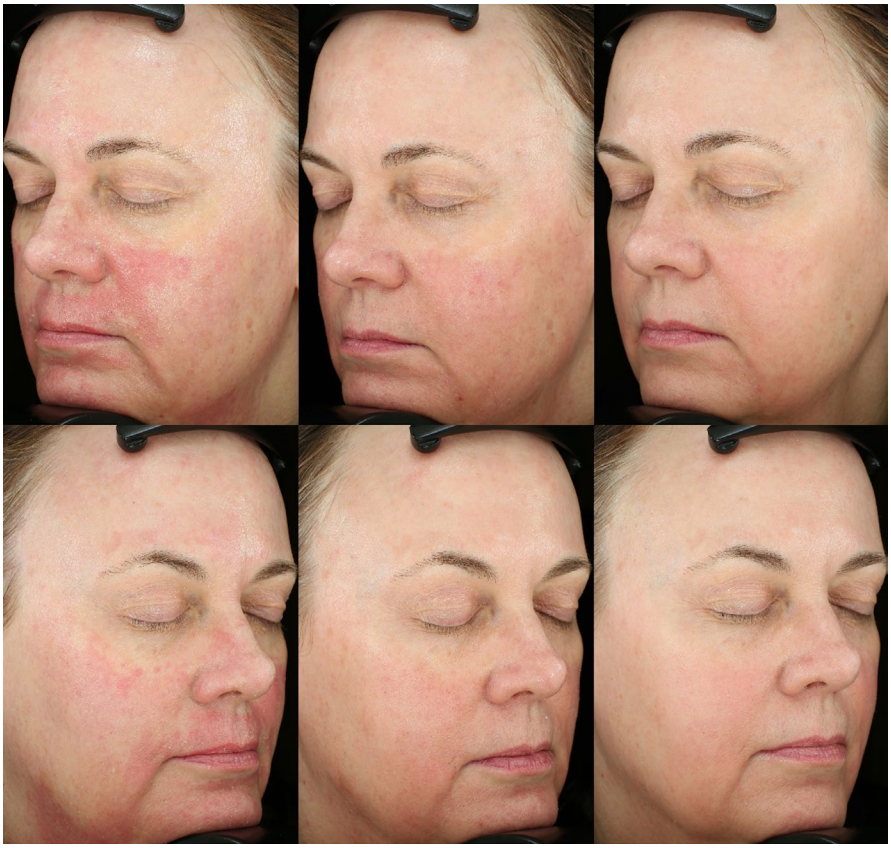

FIGURE 4 Photographs of female subject using bland moisturizer on left hemiface (top row) and TriHex serum on right hemiface (bottom row) immediately following second treatment, on post-treatment day 2, and on post-treatment day 4 (from left to right)

Tripeptide and hexapeptide serum has also shown efficacy with other laser modalities, including fractional ablative and hybrid laser resurfacing.[24,25] Within the first 2 weeks following fractional ablative resurfacing, TriHex serum was associated with less erythema, exudation, tenderness, and burning and stinging when compared to a basic regimen. In addition to improved postprocedural recovery, there was also greater subject satisfaction. When combined with hybrid lasers that utilize both ablative and nonablative technologies, TriHex serum demonstrated reduced erythema and roughness within the first week following treatment.

Our data support the utility of TriHex serum as a peri-procedural adjunct to NAFL resurfacing, which is consistent with previous evidence. The vast majority of clinical measures, including global photodamage, experienced greater improvement with the addition of RSN. The immediate recovery period also demonstrated subjective improvement. Figure 3 demonstrates decreased reaction after first NAFL treatment following preprocedural RSN and comparable recovery at post-treatment day 2 with RSN and post-treatment day 4 with bland moisturizer. Figure 4 demonstrates decreased reaction after second NAFL treatment and improved recovery with prolonged use of RSN. Overall, patients were satisfied with the product, which had no significant adverse events. These results supplement the current evidence for improved outcomes, recovery, and satisfaction from the addition of TriHex serum to the treatment regimen.

Limitations of this study include the relatively small sample size. This limited the statistical significance of the observed trends. It is likely that a larger sample size would have found more of the observed trends to be significant and similar to previous studies. Since we evaluated the peri-procedural use of RSN in combination with NAFL, which is known to already have short postprocedural downtime and limited recovery, more subjects were likely needed to statistically detect all improvements. There were also no biopsies that were involved in this study. The inclusion of biopsies would have allowed for histologic analysis of collagen and elastin in the dermis. However, multiple studies have already established the histologic improvements in collagen and elastin that TriHex Technology can offer.[10,12-15]

5 | CONCLUSION

In this randomized, blinded, split-face, comparative trial, the addition of TriHex serum as a peri-procedural adjunct to NAFL resurfacing improved various clinical measures of facial photodamage and cutaneous aging and the immediate postprocedural recovery. TriHex serum was demonstrated to be safe, well-tolerated, and well-liked by subjects.

CONFLICT OF INTEREST

Jordan Wang and Roy Geronemus are consultants for Alastin.

AUTHOR CONTRIBUTIONS

All authors contributed equally to this study.

ETHICAL APPROVAL

Informed consent was obtained from all individual participants involved in the study. All procedures performed were in accordance with the ethical standards of the IRB and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

SUBJECT PHOTOGRAPH PERMISSION

All subjects provided written consent for permission to publish their photographs.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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