

ORIGINAL CONTRIBUTION

Effects of anhydrous gel with TriHex peptides on healing after hybrid laser resurfacing

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Email: arisaortiz@gmail.com**Abstract**

Background: Hybrid fractional laser skin resurfacing is a procedure that combines fractional nonablative and ablative wavelengths to improve photoaging. The postoperative period involves overt skin swelling, redness, and roughness.

Objective: A single-center, randomized trial was performed to compare the effect of a standard Skincare regimen, with and without an anhydrous gel with TriHex peptides (a proprietary tripeptide and hexapeptide blend), on recovery after hybrid laser resurfacing of the face.

Methods: Five subjects were assigned to a split-face protocol. Use of the skin regimen began approximately 2 weeks before the hybrid laser resurfacing and ended 7 days after. Subjects were evaluated by a physician for postprocedural healing. Additionally, the subjects were photographed and completed surveys to assess postprocedural healing and overall preference for Skincare regimen.

Results: Based on physician assessment, mean redness on postoperative days 1 and 4 and mean roughness on the postoperative days 3 and 4 were significantly ($P < .05$) improved on the side of the face using the anhydrous gel with TriHex peptides compared with the side using a standard skin regimen. Based on subject assessment, 4 out of 5 subjects thought that their skin and complexion appeared better on the anhydrous gel-treated side and preferred the Skincare regimen with the gel.

Conclusions: These data suggest that using the anhydrous gel with TriHex peptides before and after hybrid fractional laser skin resurfacing can minimize the postoperative redness and roughness that are typical and expected for this procedure.

KEYWORDS

collagenesis, elastogenesis, extracellular matrix recycling, hybrid fractional laser resurfacing, peptides, postprocedure healing

1 | BACKGROUND

Skin resurfacing with conventional ablative lasers may require substantial recovery time of up to 14 days with at least 2 months of erythema.¹ During this time, the side effects are edema, erythema, and dyspigmentation.² Over the past several years, use of fractional ablative lasers have gained popularity to help correct the presence

of facial wrinkles, dyspigmentation, texture, and scarring due to their improvement in downtime and side effects compared to fully ablative lasers.² A first-in-class hybrid fractional laser uses a combination of ablative and nonablative wavelengths simultaneously.³ This approach should theoretically provide outcomes that approach ablative laser resurfacing with decreased patient downtime and severity of side effects.^{2,4}

An anhydrous gel with TriHex peptides and ancillary actives (ALASTIN Skin Nectar® with TriHex technology®, ALASTIN Skincare®, Inc, Carlsbad, CA) is designed to treat skin prior to, during, and after cosmetic procedures. Tripeptides and phosphatidylserine contained in this formulation were shown to clear damaged and aged proteins by triggering a) proteases, such as matrix metalloproteinase-2 (MMP-2) in the extracellular matrix (ECM), and b) autophagic and ubiquitin protease systems intracellularly.⁵⁻⁷ Additionally, phosphatidylserine may reduce levels of destructive proteases, that is, collagenase and MMP-1.⁸ There is evidence that the active ingredients, tripeptides, and hexapeptides, stimulate the skin to produce new collagen and elastin.⁹⁻¹¹ Other actives in the formulation, such as Dunaliella salina extract and naringenin, have antioxidant and anti-inflammatory properties, such as the ability to quench free radicals and inhibiting inflammatory cytokine production, respectively.^{12,13} Consequently, use of this gel is anticipated to accelerate the epidermal healing process when used for skin bed preparation prior to a fractional ablative procedure, as well as during and after the procedure.

We hypothesize that the anhydrous gel with TriHex peptides will shorten downtime following hybrid fractional ablative and nonablative laser resurfacing to the face. We anticipate the gel will stimulate cumulative neocollagenesis and elastogenesis, allowing the skin to recover faster following the laser surgery.

2 | MATERIALS AND METHODS

2.1 | Study design and procedure

This is a comparative split-face, single-blind, randomized study assessing the healing and outcome effect of the anhydrous gel with TriHex peptides before, during, and after hybrid fractional ablative and nonablative laser resurfacing of the face. Five subjects, ages 25-60, Fitzpatrick skin types I-III, were selected to undergo hybrid laser resurfacing treatment to the face, and each agreed to apply the skincare regimens as instructed and return for follow-up visits. Two weeks (-17 to -14 days) prior to the procedure, subjects were seen for their pretreatment visit. Pretreatment digital images were taken with the Visia photography system, and subjects were randomized to which side of their face will receive the anhydrous gel (right or left). Each subject was given a basic skincare regimen (CeraVe® Cleansing Lotion, CeraVe® Cream, and Neutrogena® Ultrasheer® SPF 30). All subjects began using the basic skincare regimen to their entire face and the anhydrous gel with TriHex peptides (ALASTIN Skin Nectar® with TriHex Technology®, ALASTIN Skincare®, Carlsbad, CA) to the assigned side of the face twice daily until their next scheduled appointment, at least two weeks from the pretreatment visit. Subjects were provided an instruction sheet that details the order of application and a diary to document and record the application.

Subjects returned to the clinic (day 0) for the hybrid laser procedure to the face. Compliance with the regimen and gel application

was confirmed through verbal report and completed diary. Again, preoperative Visia digital images were taken for each subject. Subjects were then treated with the hybrid laser procedure and Skincare regimen as described below. As with the 2 weeks prior, each subject continued to use the anhydrous gel on the randomized side of the face twice a day, with the basic skincare regimen to the entire face.

Each subject returned for follow-up on postoperative days 1, 3, 4, and 7. The subject and a physician filled out a survey evaluating the postoperative healing assessments. Full-face Visia digital images were obtained at all visits.

2.2 | Hybrid fractional laser resurfacing

Topical 7% lidocaine/7% tetracaine anesthetic was applied to each subject's face for 60 minutes prior to the procedure. The subject then underwent hybrid fractional laser resurfacing using nonablative and ablative wavelengths of 1470 and 2940 nm, respectively (Halo™ Hybrid Fractional Laser; Sciton, Inc, Palo Alto, CA). Subjects wore optical shields to ensure orbital protection at all times during the treatment. Settings for the two wavelengths area as follows: depth for the 1470-nm wavelength ranged from 400-450 micrometers, with a density of 20% and the depth for the 2940-nm wavelength was 20 micrometers with a density of 14%. Total energy was between 1800 and 2000 Joules. Immediately following the procedure (day 0), the anhydrous gel with TriHex peptides was applied to the appropriate randomized side of the subject's face. CeraVe Cream was applied to the entire face roughly 10 minutes after the application of the gel. Visia images were obtained directly after the treatment.

2.3 | VISIA imaging

As mentioned previously, two weeks (-17 to -14 days) prior to treatment, at baseline, and postoperative days 1, 3, 4, and 7, digital images were taken of each subject's face (from the center and right- and left-side). For all digital photography, the VISIA photo station (Canfield Imaging Systems, Fairfield, New Jersey) with a Canon Mark II 5D Digital SLR Camera (Canon Incorporated, Tokyo, Japan) and standard, reproducible lighting were used.

2.4 | Subject assessments

All 5 subjects participated in a preprocedural discussion about the protocol at least 2 weeks prior to laser resurfacing. At days 1, 3, 4, and 7 after the procedure, subjects filled out a survey assessing their opinion on the redness, swelling, roughness, pain, heat, and dryness for the anhydrous gel-treated and the standard regimen-treated side of the face. The scores ranged from 0 to 5, with 0 representing no appreciable change in the skin compared with baseline, and 5 representing a severe, maximal amount of the quality in question.

2.5 | Physician postprocedural assessment

A blinded physician assessment was also obtained at each postoperative follow-up visit (days 1, 3, 4, and 7). The physician evaluated redness, swelling, and roughness. The scores again ranged from 0 to 5, with 0 representing no appreciable change in the skin compared with baseline, and 5 representing a severe, maximal amount of the quality in question. The means for each side of the face, treated with or without the anhydrous gel with TriHex peptides, were calculated. To determine the statistical significance of the means for the different treatments, the paired sample Student's *t* test was used with the cutoff of $P < .05$ for significance. The one-tailed significance test was used to investigate whether use of the gel with the basic regimen had a lower score than the basic regimen alone.

3 | RESULTS

3.1 | Subject postprocedural assessment

Each subject underwent the hybrid fractional laser resurfacing of the facial skin without complication. Based on each subject's assessment, there was no significant difference in redness, swelling, roughness, pain, heat, or dryness when comparing the side with versus without application of the anhydrous gel with TriHex peptides during any day of the postprocedural follow-up. One of 5 subjects felt that postoperative redness (days 1 and 3) and roughness (days 1, 3, and 4) were improved on the anhydrous gel-treated side compared with the standard regimen-treated side (data not shown).

3.2 | Blinded Physician postprocedural assessment

The day 1 assessment was statistically significant ($P < .05$) for a lower mean redness on the side of the face with versus without application of the anhydrous gel with TriHex peptides (Figures 1 and 2). Three of 5 subjects had decreased redness on the gel-treated side compared with the standard regimen-treated side. Edema and roughness on day 1 were equivalent.

Analysis of postoperative day 3 revealed that there was decreased roughness and a statistically significant ($P < .05$) lower mean score on the gel-treated side compared with the standard regimen-treated side of the face. One of the subjects was unable to come for assessment on day 3, but 3 out of 4 subjects evaluated showed reduced roughness on the side using the anhydrous gel with TriHex peptides (Figures 1 and 2). Additionally, on the gel-treated side, out of 4 subjects, 1 subject had reduced redness and another had less edema (Figure 2). Finally, based on physician assessment, the skin in all subjects was either equivalent or improved compared with the standard regimen-treated skin.

Data from evaluations day 4 postprocedure were also in favor of the skin with the applied anhydrous gel with TriHex peptides. On day 4, physician assessment found that the mean score for redness was



FIGURE 1 Two representative subjects are shown 4 days post-laser resurfacing. Using a split-face model, the assessing physician found the gel-treated side displayed decreased erythema and roughness compared with the side treated with only the basic skin regimen

statistically improved on the gel-treated side of the face ($P < .05$); redness was improved in 4 out of 5 subjects (Figure 2). For the subjects that were still experiencing mild swelling, 2 out of 5 subjects, both of the subjects had less swelling on the side of the face with versus without application of the anhydrous gel with TriHex peptides. Lastly, on day 4, the mean score for roughness was significantly improved ($P < .05$; 3 out of 5 subjects had less roughness) on the gel-treated skin. Similar to findings on day 3, the standard regimen-treated side of the face did not show superiority in the 3 aspects assessed in any of the 5 subjects. On day 7 post-treatment, all 5 subjects had recovered fully from the hybrid fractional laser skin resurfacing with no appreciable redness, swelling, or roughness on either side of the face when compared with preprocedural assessment.

3.3 | Subject skin regimen assessment

On days 1, 3, 4, and 7, subjects were given skin regimen assessments which evaluated the subjects' opinions on the regimens that they had engaged in for at least 3 weeks. On day 1, though not necessarily reflected in the subjects' postoperative assessments, 3 out of 5 felt that their skin and complexion looked better on side of the face with versus without application of the anhydrous gel with TriHex peptides (Figure 3). By day 3, four out of the 5 subjects felt that their

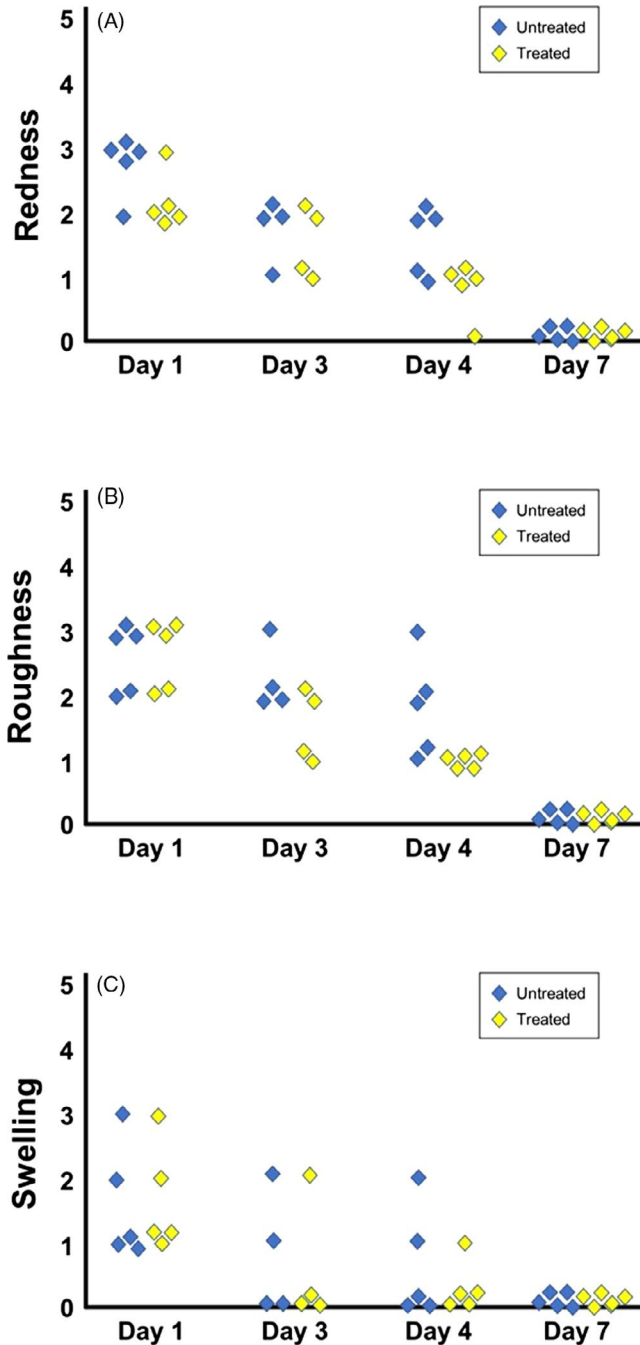


FIGURE 2 The physician postoperative assessment of redness, swelling, and roughness over 1 week is plotted in the following charts with a point representing the score for each subject and each Skincare regimen. There was a significant ($P < .05$) improvement in the mean redness (A) of the sides of the face treated with the anhydrous gel with TriHex peptide at 1 and 4 days post-laser resurfacing compared with the sides treated with only the basic skin regimen. Mean roughness (B) was also significantly decreased ($P < .05$) at both 3 and 4 days after resurfacing on the gel-treated side of the face. Swelling was not significantly altered throughout the post-resurfacing recovery period (C)

skin and complexion looked better on the gel-treated side and 3 out of 5 reported that the gel-treated skin also felt better. Assessment on day 4 revealed again that 3 out of the 5 subjects believed their

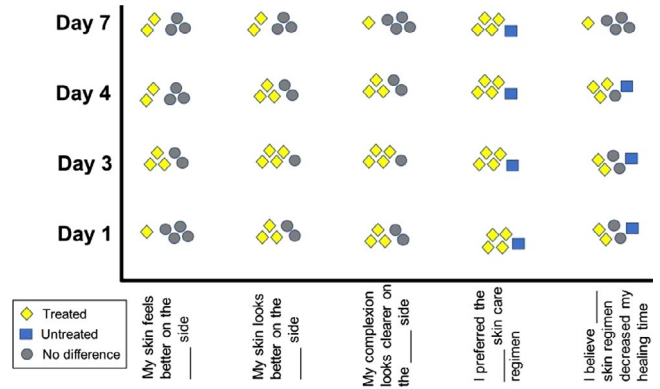


FIGURE 3 The subject facial skin assessment over 1 week is plotted with a symbol for each subject and color-coded by preference to Skincare regimen. Overall, subjects noted improved skin appearance and complexion on the side with the anhydrous gel with TriHex peptide applications. Four out of 5 subjects preferred the regimen containing the anhydrous gel with TriHex peptides

skin and complexion looked better on the side with application of the anhydrous gel with TriHex peptides and importantly, 3 out of the 5 subjects believed that the regimen containing anhydrous gel with TriHex peptides helped decrease the healing time after the hybrid fractional laser skin resurfacing. Overall, at all 4 time points, 4 out of 5 subjects preferred the gel-containing skin regimen, and only 1 out of 5 preferred the basic skin regimen.

4 | DISCUSSION

Hybrid fractional laser, which combines ablative and nonablative wavelengths, is an excellent option for skin resurfacing with improved downtime. Though the post-treatment healing time is reduced compared with ablative resurfacing,^{3,4} there still remains a week of redness, swelling, and roughness with hybrid fractional resurfacing.

In this study, the use of the anhydrous gel with TriHex peptides before a laser resurfacing procedure is novel. The “skin bed preparation” approach, which prepares the skin for the laser resurfacing wounds, is an approach not typically taken in current practice.¹⁴ The anhydrous gel contains TriHex peptides and phosphatidylserine that help clear the ECM of degraded and agglutinated proteins during this preparatory phase.⁵⁻⁷ Once the skin is prepared by clearing the ECM, the proprietary combination of peptides, which stimulate the skin to produce new collagen and elastin,^{9,11,15} may potentiate healing after the laser resurfacing wounds. Furthermore, other actives in the anhydrous gel with TriHex peptides, such as Dunaliella salina extract and naringenin, have antioxidant properties which may decrease inflammation and irritation,⁹⁻¹¹ resulting in an accelerated epidermal healing process.¹⁵

For the blinded physician postoperative assessment, our data showed that on day 1, redness was significantly decreased on the side of the face with application of the anhydrous gel with TriHex peptide, compared to the side without. On day 3, the most pronounced finding was significantly reduced roughness on the gel-treated skin,

compared with the standard regimen-treated skin. Additionally, on day 4, roughness, redness (these 2 parameters showed statistical significance), and any residual swelling were also improved on the side of the face with application of anhydrous gel with TriHex peptide. Four out of 5 subjects preferred the gel-containing treatment regimen. Finally, on day 3, 4 out of 5 subjects felt that their skin and complexion looked better on the side with application of the anhydrous gel with TriHex peptide.

5 | CONCLUSION

Based on these data, use of an anhydrous gel with TriHex peptide 2 weeks before and 1 week after a hybrid fractional laser resurfacing of the face did improve the speed of postoperative healing. The most notable results with the anhydrous gel with TriHex peptides were decreased redness and roughness. These results did not compromise the overall resurfacing outcome. Moreover, a majority of the subjects preferred using the gel compared with a standard skincare regimen. Use of the anhydrous gel with TriHex peptides prior to and during recovery from hybrid fractional laser resurfacing may be advantageous to patients who need to minimize time away from their daily routine and responsibilities.

DISCLOSURES

Dr Arisa Ortiz is a paid consultant to Alastin SkinCare®, Inc

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