A Multi-Center Evaluation of Restorative Eye Treatment and INhance With Trihex Technology to Improve Aesthetic Outcomes When Used Pre- and Post-Blepharoplasty

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Abstract
Background: Restorative Eye Treatment with TriHex Technology (RET) is a topical eye product with peptides and botanicals that reduce the appearance of crow’s feet, under-eye bags, and dark circles. INhance with TriHex Technology (IH) is a topical product that has been clinically proven to accelerate the clearance of bruises and aid in the reduction of swelling. TriHex Technology has been shown to regenerate collagen and elastin.

Objectives: Evaluate the use of RET compared to a bland moisturizer prior to blepharoplasty and the bilateral use of INhance postoperatively.

Methods: Blepharoplasty patients were randomized to use either RET or a bland moisturizer, twice daily, on the designated periocular skin for 4 weeks prior to the procedure. Postoperatively, participants applied IH bilaterally, at least 4 times a day, and returned for follow-up on Days 1 or 3, 7, and 14. The removed upper-eyelid skin (13 patients) underwent independent dermatopathological evaluation.

Results: Investigators noted no differences in peri-operative complications but observed faster improvement in swelling, bruising, discomfort on the treated side. 85% of participants had less edema and bruising on the RET pretreated side. Biopsy results revealed improved extracellular matrix appearance on the RET pretreated side. Participants agreed that IH alleviated their swelling and noted that their skin felt and appeared more hydrated.

Conclusions: A regimen designed for eyelid surgery employing a pretreatment product component and a post treatment product appear to have a positive impact on measured outcomes in blepharoplasty patients including effects on bruising, swelling and patient comfort.

Level of Evidence: 4

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Oculoplastic surgery may be performed to correct a medical issue or for aesthetic purposes. Common postprocedure recovery includes bruising and swelling.

TriHex Technology is a unique combination of tripeptide, hexapeptide, and other active agents within a specified formulation that promote neocollagenesis and neoelastogenesis, which has been shown via histology.\(^1\) Restorative Eye Treatment with TriHex Technology (RET) is a topical eye product with peptides and actives which has shown clinically, an overall improvement in periorcular skin and a significant decrease in fine lines, under-eye hollowing, under-eye bags, and dark circles with participants noting a significant overall improvement in the appearance of the skin around the eyes.\(^2\)

INhance with TriHex Technology is a topical product that has been clinically proven postprocedures to accelerate the clearance of bruises and aid in the reduction of swelling.\(^3\) This study aimed to determine the benefits of a topical eye product used on one side preprocedure compared to a bland moisturizer on the other side to determine differences within the skin, after 4 weeks of use. Postprocedure, a separate product was applied bilaterally to assess for efficacy in bruising, swelling, and patient satisfaction.

**METHODS**

Before initiation, this multi-center, randomized, blinded study was approved through Integ Review Institutional Review Board (Austin, TX). The study was conducted from November 2020 to July 2021. Eligible participants were men and women that were undergoing a blepharoplasty and willing to refrain from the use of additional treatments, procedures, or topicals on the face during the course of the study. Participants were excluded that had been using topical products in the procedural area within 1 month of participation, had a previous hypersensitivity to any of the actives in the study products, had recent excessive sun exposure, history of keloid or hypertrophic scars, and women that were pregnant, lactating, or planning on becoming pregnant.

Participants were randomized to apply RET (Alastin Skincare, Inc., Carlsbad, CA) and a bland moisturizer (Cetaphil Lotion, Galderma, Fort Worth, TX), twice daily, on the designated right or left periorcular skin for 4 weeks prior to the procedure. All products were packaged in non-identifiable identical containers so the patient and the investigators were blind to the product being used. At surgery, the excised upper-eyelid skin was sent to an independent dermatopathologist for staining and evaluation. Postoperatively, participants applied INhance—IH (Alastin Skincare, Inc., Carlsbad, CA) immediately bilaterally to the periorcular skin, at least 4 times a day, and returned for follow-up on Days 3, 7, and 14. At every visit, standardized photography was performed and on Day 14 postop, the participants completed a questionnaire assessing the use of INhance. Written consent was provided, by which the patients agreed to the use and analysis of their data.

**RESULTS**

Eleven females and 2 two males with a mean age of 60 years completed the study. Age range was 41–93 years. Eight patients had a bilateral upper-eyelid blepharoplasty, 1 patient had a combined upper-eyelid blepharoplasty with external levator resection, and 4 patients had a bilateral upper and lower blepharoplasty. Investigators used 2% lidocaine with 1:100,000 epinephrine and no complications were reported in this series. Each investigator used their own standard postop care including the following: depending on clinical site and procedure: antibiotic ointment for 1 week, lubricant drops in the eyes as needed, antibiotics for 5 days, steroid dose pack, cold compresses for 1–2 days, head elevation, activity restriction, and avoidance of blood thinners for 1-week postop, and suture removal at 1-week postop. All patients returned for follow-up on Days 3, 7, and 14, with an average follow-up of 35 minutes for each patient.

**Investigator Assessment and Photography**

Investigators noted that there were no differences in intra-op or postop complications but observed a faster improvement in swelling and bruising on the side pretreated with RET. This was further evaluated through photography, as 85% of participants had less edema and bruising on the side that was pretreated with RET (Figure 1).

**Post Procedure Investigator Observations With INhance Compared to Other Patients Not Using INhance With TriHex Technology**

**Site 1**

Patients noticed less bruising/swelling and felt soothing from the application process.

**Site 2**

Investigators reported less bruising, the early bruises resolved much more quickly than in patients not using IH.

**Site 3**

Investigator noticed a mild improvement in bruising and swelling in patients who used IH. Comfort level is no
different, as there is really no discomfort associated with upper-eyelid blepharoplasties.

**Participant Questionnaire**

Of the participants that experienced postop edema, 89% strongly agreed or agreed that IH alleviated their swelling. Of the participants that experienced postop ecchymosis, 91% strongly agreed or agreed, that IH alleviated their bruising and 91% of participants strongly agreed or agreed that their skin felt and appeared more hydrated. All the participants liked the way the product felt when applied.

**Biopsies**

Thirteen upper-eyelid specimens were collected within the study. On one side, RET was applied and on the other side, a bland moisturizer for up to 4 weeks presurgery. An independent dermatopathologist (Laboratory & Pathology Diagnostics, Naperville, IL) blinded to the treatment received before surgery, completed the analyses. Hematoxylin & Eosin; Herovici and Movat stains were performed and a dermatopathologist compared sides with particular reference to extracellular matrix (ECM) health, neocollagenesis and neoelastogenesis. In 13 of 15 cases (87%), the changes showed remarkable consistency —healthier ECM, younger and more plentiful collagen and elastin; 2 cases showed no difference (Table; Figure 2).

**Safety**

There were no reported adverse events.

**DISCUSSION**

This study aimed to determine whether topical pretreatment of the eyelids prior to a blepharoplasty procedure improved postoperative recovery. In addition, a postoperative treatment formulation was used to determine the impact on postoperative bruising, swelling, and discomfort. The use of a topical eye product used on one side preprocedure was compared to a bland moisturizer on the other side to determine differences within the skin quality and appearance and postblepharoplasty recovery, after 4 weeks of use.

This study demonstrates that this treatment appeared to have made a difference in 85% of patients undergoing blepharoplasty surgery. Qualitative and subjective analysis demonstrated reduced edema, swelling, less bruising, and less patient reported discomfort. The postoperative regimen used was identical on both sides so the differences noted were attributed to the pretreatment application. TriHex technology has been used extensively as pretreatment “preparation of the surgical canvas” in numerous clinical trials with improved outcomes demonstrated. The scientific premise which has been demonstrated with gene expression, biopsies, in vitro testing, and clinical trials demonstrate that the active agents within the formulation recycle the contents of the ECM promoting a renewal and replacement of the structural proteins (collagen and elastin), renewal of basal stem cells, and thickening of epidermal and barrier layers. This translates into improved cellular protein cross talk with the ECM, thus optimizing healing patient outcomes. The product used postoperatively has been developed to decrease swelling and bruising based on actives that improve macrophage function in relation to red blood cell phagocytosis.
Limitations in this study include a heterogenous group of surgical patients, one-third of whom underwent lower as well as upper blepharoplasty, the small number and a double product evaluation, all of which may conclusions more difficult. That noted the positive investigators’ impressions, particularly relating to patients that were pretreated with active product suggest an advantage of hastened recovery in this pretreated group of patients. In addition, biopsy outcomes provide an objective confirmation of the changes seen at a molecular level which provide good evidence for the clinical improvements reported. In this regard, the emphasis of this study and its analysis concern the concept of surgical preconditioning, an approach that is being adopted more and more in the surgical realm. This is a

### Table Summary of Histology Findings

<table>
<thead>
<tr>
<th>Patient label</th>
<th>Improved dermal extracellular matrix</th>
<th>Healthier collagen deposition</th>
<th>Healthier Elastin deposition</th>
<th>Healthier Epidermis (rete pegs)</th>
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</table>

ND, no difference; RET, restorative eye treatment.

![Figure 2. Typical example of histology differences in the same patient: (A, B) Hematoxylin and Eosin (H/E) staining—healthier extracellular matrix (ECM) with new wavy, organized collagen fibers (rectangle) on (A) RET side. (C, D) Herovici stains showing significant mucopolysaccharides (MPS) and new collagen fibers in (C) papillary dermis (rectangle) RET side compared with (D). (E, F) Movat stain demonstrating dense layers of new elastin deposition in papillary dermis E (rectangle) compared with (F). RET, restorative eye treatment side.](https://academic.oup.com/asjopenforum/article/doi/10.1093/asjof/ojac089/6895721)
differentiating feature that can contribute to the knowledge base of current literature.

**CONCLUSIONS**

In conclusion, a regimen designed for eyelid surgery employing a pretreatment product component and a post-treatment product appear to have a positive impact on measured outcomes in blepharoplasty patients including effects on bruising, swelling, and patient comfort.

**Disclosures**

Dr Widgerow is the chief scientific officer of Galderma (Lausanne, Switzerland). Dr Widgerow and Ms Bell are employees of Galderma, both were involved in collating data and paper writing. There was no involvement in the actual trial. The remaining authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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**REFERENCES**


