

## CORNEA/EXTERNAL DISEASE

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### Corneal haze after collagen cross-linking diminishes over time

Researchers help define time course for wound healing.

Corneal haze caused by collagen cross-linking in patients with keratoconus or ectasia after LASIK takes at least 1 year to resolve but does not affect clinical outcomes, a study found.

According to Peter S. Hersh, MD, FACS, corresponding study author, the goal of the study was to evaluate the corneal wound healing process after collagen cross-linking.

“We wanted to specifically illustrate the time course of wound healing after the procedure,” Dr. Hersh told *Ocular Surgery News*. “As we saw from the main outcome indicators, there is a time course to improvement, likely secondary to wound healing.”

Dr. Hersh said the researchers also wanted to quantitate corneal haze, which is identified as a dust-like change in the stroma or as a mid-stromal demarcation line. Its appearance after cross-linking has a different clinical appearance than haze after other procedures, according to the study.

The results were published in the *Journal of Cataract and Refractive Surgery*.

#### Methods, patients

The prospective, randomized, controlled multicenter clinical trial included 50 eyes of 44 patients who underwent standard corneal collagen cross-linking with topical riboflavin and ultraviolet A light. Of the 50 eyes, 31 had keratoconus and 19 had ectasia.

Eyes with corneas thinner than 400  $\mu\text{m}$  were swelled with hypotonic riboflavin drops until the stroma measured more than 400  $\mu\text{m}$ . After the procedure, Pentacam Scheimpflug densitometry (Oculus) and slit lamp biomicroscopy were used to measure haze.

The study also included a control group of 41 eyes that received only riboflavin initially. These patients underwent the full cross-linking procedure after 3 months.

Follow-up was conducted at 1, 3, 6 and 12 months.

The treatment and control groups were analyzed as cohorts and then individually within keratoconus and ectasia subgroups.

#### Results

Mean corneal densitometry peaked at  $23.4 \pm 4.4$  at 1 month after the procedure. Although no significant change was observed between 1 and 3 months, densitometry began to decrease between 3 months and 6 months, with a more significant decrease in the ectasia group.

At 1 year, a significant difference in corneal haze was observed between the two groups. The mean densitometry remained slightly increased from  $14.6 \pm 2.1$  at baseline to  $17.5 \pm 4.4$  in the keratoconus group, while the ectasia group returned to baseline. Similar analysis using observer-graded slit lamp haze corroborated the densitometry haze results.

Eyes treated with hypotonic riboflavin did not show any differences from those that did not require swelling.

Dr. Hersh said that he can only speculate about why haze clearing varied between the subgroups but said that it is possible that keratoconus and corneal ectasia are “separate and distinct disease entities” that respond to cross-linking differently.

He added that the LASIK flap and the flap interface in ectasia could contribute to the differences in initial response and subsequent healing, as well as haze formation and haze clearing after the procedure.



Peter S. Hersh

## Conclusions

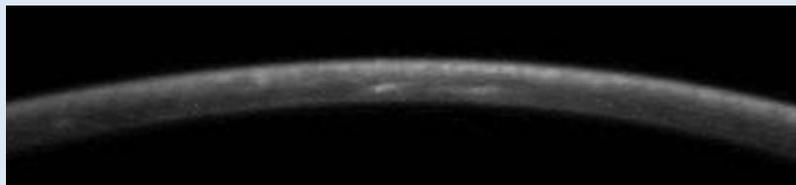
The occurrence of cross-linking-associated corneal haze did not appear to affect clinical outcomes. Dr. Hersh said the researchers found no significant correlations in terms of stability, maximum keratometry, or uncorrected or corrected visual acuity.

“[Haze] seems to be something that simply is an expected clinical sign of the wound healing process that goes on after cross-linking,” he said. “Surgeons new to cross-linking should be aware of this finding and the expected time course of cross-linking-associated corneal haze.”



Corneal cross-linking haze.

Images: Hersh PS



Haze seen with Scheimpflug system.

To minimize haze, he suggested proper supervision of the ocular surface postoperatively, which includes managing the bandage contact lens to assure rapid epithelialization, as well as appropriate removal of the contact lens after healing.

Dr. Hersh and colleagues plan to conduct another multicenter trial that will examine possible changes in the cross-linking process that could make the procedure faster.

They are also currently analyzing the study group reported here to compare hypotonic riboflavin treatment with the standard dextran formula, as well as variables that could influence outcomes and the wound healing process, such as age, sex, corneal thickness, keratoconus severity, topography features and preoperative vision.

Dr. Hersh said he hopes to determine the characteristics that create better or worse outcomes for patients. – *by Courtney Preston*

## Reference:

- Greenstein SA, Fry KL, Bhatt J, Hersh PS. Natural history of corneal haze after collagen crosslinking for keratoconus and corneal ectasia: Scheimpflug and biomicroscopic analysis. *J Cataract Refract Surg.* 2010;36(12):2105-2114.
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  - Disclosure: Dr. Hersh is medical monitor to Avedro Inc.
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## PERSPECTIVE

Riboflavin UV cross-linking has become a mainstream treatment for ectatic corneal disease around the world. In fact, the United States is the only industrialized country that does not routinely perform this sight-saving procedure. One of the common findings in patients who have undergone cross-linking is the development of corneal haze, which can be significant at times. Greenstein and colleagues have shown that the corneal haze associated with riboflavin UV cross-linking peaks at 1 month, plateaus at 3 months and then improves thereafter. Of note is the finding that corneal haze is not correlated with visual recovery. The authors have provided useful information for the clinician and patient that demonstrates that corneal haze after cross-linking is transient, not vision-threatening and markedly improves with time.

– **Eric D. Donnenfeld, MD**

OSN Cornea/External Disease Board Member

Disclosure: Dr. Donnenfeld has no relevant financial disclosures.