Early outcomes positive for cross-linking, corneal implant treatment for keratoconus and ectasia

No statistically significant differences between combined and sequential procedures have been observed.

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Peter S. Hersh

Combining corneal collagen cross-linking with a corneal implant may provide a new way to treat keratoconus and corneal ectasia, according to a physician.
At the American Academy of Ophthalmology meeting, Peter S. Hersh, MD, FACS, presented preliminary results of a single-center, prospective, randomized clinical trial for treatment of keratoconus and corneal ectasia using Intacs (Addition Technology) combined with corneal collagen cross-linking.
"Intacs and cross-linking have different goals in the treatment of keratoconus and ectasia," Dr. Hersh, OSN Refractive Surgery Board Member, said in a follow-up interview. "The goal of Intacs is to flatten the cone and make the corneal topography more symmetric. The goal of cross-linking is to decrease the natural progression of these disease processes."
The clinical trial reported by Dr. Hersh investigated the combined use of Intacs and cross-linking, specifically looking at the timing of the two procedures.

Collagen cross-linking
"The published results of collagen cross-linking and the number of clinical trials that have been undertaken both in Europe and Australia have been very encouraging," Dr. Hersh said. "In the U.S., cross-linking is not approved, but a multicenter clinical trial on cross-linking, sponsored by Avedro Inc., has been completed, and data recently have been submitted for potential U.S. Food and Drug Administration approval."
Cross-linking consists of 365 nm of ultraviolet light interacting with riboflavin eye drops, "which causes the riboflavin molecule to activate into a higher energy state," Dr. Hersh said. "This activated riboflavin also interacts with oxygen in the system, causing the production of reactive oxygen species."
The activated riboflavin and the reactive oxygen species interact with the cornea as well "in order to form cross-links either between collagen molecules or between collagen molecules and the stromal matrix of the cornea," said Dr. Hersh, who has performed approximately 300 cross-linking procedures.
By cross-linking collagen molecules, the cornea is biomechanically stiffened, thus strengthening the keratoconic or ectatic cornea with the goal of stabilizing disease progression.

Early study results
The study, performed under an investigational review board-approved single-center physician-sponsored IND, is ongoing and has an estimated enrollment of 160 patients. Dr. Hersh performed all the procedures.
There were two arms to the study. One involved the insertion of the corneal implant followed by cross-linking within the same treatment session (combination treatment), and the other involved

insertion of the corneal implant followed 3 months later by cross-linking (sequential treatment). The cross-linking portion of both arms involved a riboflavin drop every 2 minutes for a total of 30 minutes after epithelial debridement and then UV light exposure with an additional riboflavin drop every 2 minutes for another 30 minutes. For standardization, all patients received two symmetric 350-µm Intacs segments.

"We want to ascertain the best timing of Intacs and cross-linking," Dr. Hersh said. "Our aim is to help keratoconus in two ways: stabilization with cross-linking and improve corneal topography with Intacs, as well as ultimately improve contact lens fit and spectacle corrected vision with Intacs."

At 6 months postop, data were available for 29 treated eyes: 16 eyes (12 keratoconus, four ectasia) were in the combination group, and 13 eyes (nine keratoconus, four ectasia) were in the sequential group.

"Early results show that the procedure is safe when done together," Dr. Hersh said. "We have had no untoward major complications, and we have not been able to find a statistically significant difference between doing the procedure as combined or sequential."

Uncorrected visual acuity, best corrected visual acuity and keratometry were examined.

"Although we found better uncorrected visual acuity improvement by 2.5 lines of logMAR visual acuity in the combined group, compared with about 1.5 lines in the sequential group, these results were not statistically significant," Dr. Hersh said. "However, we need to await more numbers and greater follow-up to see if there is a true difference."

BCVA improved the same in both groups, as did corneal flattening.

There were no statistically significant differences between the two groups at 1 year, for which data were available for 15 treated eyes.

Improvement after surgery

"The time course of cross-linking, per se, is that patient vision and patient topography tend to worsen slightly at 1 month after the cross-linking, then improve thereafter," Dr. Hersh said. "This is likely secondary to the epithelial and stromal wound-healing course that cross-linking itself causes."

With the implant alone, "patients generally get immediately better," Dr. Hersh said. "But when we superimpose the cross-linking on top of the Intacs, it slows down the Intacs' response somewhat."

Dr. Hersh said that the entire process of cross-linking may take 6 to 12 months to fully stabilize. Outcomes reported in international studies out to 6 years show relatively good stability, he said.

– by Bob Kronemyer

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- Disclosure: Dr. Hersh receives research support from Addition Technology. He is the paid medical monitor for Avedro, which makes products used in corneal collagen cross-linking.