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Corneal collagen cross-linking may help with keratoconus

Clinical

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NEW YORK (Reuters Health) - Corneal collagen cross-linking (CXL) helps control keratoconus progression in all age groups, but it works best in adults under 40, new data suggest.

The procedure involves a photo-oxidative reaction, catalyzed by riboflavin, that stiffens the cornea. The biomechanical change leads to improvements in visual acuity and function, researchers explained in a January 3 online report in *Ophthalmology*.

In their new study, corneal CXL was beneficial for children and adults, with the best results in patients ages 18 to 39.

"This information could be valuable for the ophthalmic surgeon when selecting appropriate patients and predicting the outcomes of this procedure for the treatment of keratoconus," wrote the authors, led by Dr. Paolo Vinciguerra of Humanitas Clinical and Research Center in Rozzano, Italy.

Dr. Elmer Tu, a clinical expert affiliated with the American Academy of Ophthalmology, told Reuters Health by email, "The most important findings of the study are that, on average, patients between 18-39 with documented progression of their keratoconus who have epithelium-off collagen crosslinking will not have significant progression over the following two years and may have improvement in their best corrected vision, although not consistently so."

Dr. Tu, who directs the Cornea Service of the University of Illinois Chicago, School of Medicine and who wasn't involved in the new study, added that currently there are no good alternative treatments to stabilize keratoconus.

"Collagen-crosslinking is a treatment option that in short- and intermediate-term studies appears to be relatively safe with some short-term improvement in cornea steepening and, to a lesser extent, vision," he said.

The paper by Dr. Vinciguerra and his colleagues reviews outcomes of corneal CXL to treat progressive keratoconus, by age group, at their hospital.

As they explain the process, "After removal of the epithelium, the cornea was irrigated for 30 minutes with a solution of 0.1% riboflavin and 20% dextran, followed by irradiation with an ultraviolet A light of 3 mW/cm² for 30 minutes."

Altogether they treated 400 eyes of 301 patients, including 49 eyes of patients ages nine to 17 (12.25%), 185 eyes of patients ages 18 to 29 (46.25%), 115 in patients in their thirties (28.75%), and 51 in patients 40 or older (12.75%).

They had follow-up data for 54% of patients at one year, 13% at two years, 5% at three years, and 2% at four years.

After 12 months, best-corrected visual acuity (BCVA) had increased significantly in the children and adolescents by a mean reduction of -0.11 logarithm of the minimum angle of resolution (logMAR).

After 36 months, significant increases in BCVA were seen in the 18-to-29-year-olds (by -0.31 logMAR), in the 30-to-39-year-olds (by -0.33 logMAR), and in the 40-and-older group (by -0.26 logMAR).

Corneal shape was regularized with a significant reduction of opposite sector index by a mean value of -0.53 at 12 months in the youngest group, by -1.14 at 36 months in the younger adults, by -1.10 at 36 months in the 30-to-39-year-olds, and by -0.55 at 12 months in the oldest patients.

Optical quality was improved by a mean significant reduction of coma -1.52 mcm after 12 months in the children and teens, -1.58 mcm after 24 months in the young adults, -2.57 mcm after 36 months in the 30-to-39-year-olds, and -0.25 mcm after 36 months in older patients.

While other treatments for keratoconus aim to replace the ectatic tissue or to remodel it, corneal CXL uses a completely different approach, the authors note - and an expert not involved in their study told Reuters Health corneal CXL is safer than traditional surgery.

"Crosslinking with the use of riboflavin in the treatment of keratoconus seems a much more viable and safer treatment than the use of penetrating keratoplasty (PK). The use of riboflavin is a much more innocuous approach than PK," said Dr. Morton Waitzman, emeritus professor of ophthalmology at Emory University in Atlanta, Georgia, in an email.

According to the authors, their results suggest that corneal CXL induces corneal stability even beyond the estimated two to three years necessary for corneal collagen turnover. They speculate that this may be due to changes in the characteristics of the keratocyte population, to a slower turnover of crosslinked fibrils, or to the possibility that the corneal collagen turnover is slower than estimated.

"The authors note that worsening of keratoconus in those patients under 18 is usually more aggressive and that this may be more difficult to treat with collagen crosslinking. This suggests that either this population may not benefit as much from collagen cross-linking, or that the treatment technique may need to be more aggressive in order to stabilize these eyes," said Dr. Tu.

"On the other hand, older patients, especially those first diagnosed with keratoconus at an older age, usually progress less aggressively, making differences harder to demonstrate," he added.

"Finally, both groups were much smaller than the main groups. All of these factors would make it more difficult to show a benefit in these two groups," he said.

Dr. Tu noted that foremost among the questions that remain about crosslinking and keratoconus is long-term stability.

"Keratoconus is a difficult disease to study because its course is highly variable in amplitude and pace of progression. It's a disease that may progress in fits and starts, often differently in each eye, which is often impossible to predict. Practically, if an individual patient does well for a couple of years, it is difficult to know whether it was the treatment or just natural history," he said.

"Short term studies are encouraging, especially from a safety standpoint, but without either large scale studies, long-term follow-up, or both, we won't be able to know definitively" what the course of disease after treatment will look like, he concluded.

Dr. Vinciguerra did not respond to a request for comments.

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