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Podcast 5

CORNEAL COLLAGEN CROSS-LINKING AND KERATOCONUS

Introduction.
This series of podcasts is hosted by the Vision Center of Excellence, a joint program of the Department of Defense and Department of Veterans Affairs.

The podcast series provides concise summaries of issues and reports targeted to Department of Defense and Veterans Affairs vision providers overseeing care for our Service members and Veterans.

Body.
This podcast summarizes and comments on two articles published in *Ophthalmology*. The first is titled "Corneal Collagen Cross Linking with Riboflavin and Ultraviolet-A Irradiation for Keratoconus", and is co-authored by Dr. Hassan Hashemi and colleagues and published in August 2013. The second article, co-authored by Dr. Christine Wittig-Silva and colleagues, is titled "A Randomized, Controlled Trial of Corneal Collagen Cross-Linking in Progressive Keratoconus" and was published in January 2014.

Keratoconus is a bilateral, asymmetric and progressive disease in which the normally round, dome-like cornea becomes thin and develops a cone-like bulge. Once the cornea becomes distorted, it does not return to its normal shape. Unlike other eye diseases or vision problems that occur later in life, this disorder has a much earlier onset seen in the teens, twenties and thirties. The early prevalence of this disease affects a population that is comparable to the active duty US military force. Management of keratoconus is dependent on the severity of the disease, which makes timing of diagnosis critically important. In more severe cases of keratoconus, where other interventions such as contact lenses are not effective, a corneal transplant may be required. Historic and existing treatments focus on improving quality of vision and halting progressive vision loss; however, the search continues for more effective treatments that address long-term degeneration and halt its progression. One of these newer treatments is called Corneal Collagen Cross Linking or CXL. The two reports by Hashemi and colleagues and Wittig-Silva and colleagues both examine CXL and its efficacy in treating keratoconus. The results of each of these studies show positive long-term outcomes that support this novel treatment.

The study by Hashemi and colleagues includes data on the five-year stability of keratoconic eyes treated with CXL. The authors point out that there are few long-term studies that evaluate this method. In this study, 40 eyes of 32 patients with progressive keratoconus were treated with CXL no later than one month after baseline eye exams. All eyes were monitored for any signs of disease progression. Patients ranged in age from 15 – 35 years and 65 percent were male, a patient sample similar to the US military active duty force. Patients were tested for various measures, including both best and uncorrected visual acuity as well as maximum keratometry levels. Eyes were tested at one, three and six months as well as one, two, four and five years after the initial CXL treatment. The authors report that at the five-year mark, there was significant improvement in best corrected visual acuity compared to baseline. Corneal thickness, uncorrected visual acuity and maximum keratometry showed no significant change over the same time period. Based on findings across measures, the authors concluded that CXL may stop disease progress.

The study done by the Witting-Silva group evaluated 46 CXL-treated eyes and 48 non-treated control keratoconic eyes. The patients examined in this study were between 16 – 50 years of age, similar to the US active duty population. The patients' eyes and progression of the disease were followed for three years. After analyzing the data, the treated group demonstrated stabilization of the disease, with substantial improvement in both best- and un-corrected visual acuity as well as maximum simulated keratometry values at one, two and three years. In comparison, third-year data from the untreated group displayed a progressive worsening of their keratoconus, with significant decreased uncorrected visual acuity and increased maximum simulated keratometry values. The results of this study show the ability of CXL to halt disease progression. This study was unique because most studies to date did not utilize a control group when studying the effects of CXL.

Results in both studies showed that there was stabilization of the disease process and in some cases, an improvement in overall visual acuity. Variation in results may be attributed to differences in amount of eyes evaluated as well as the devices used to calculate curvature. Both groups of researchers agree that there are some limitations to the CXL treatment. Not every patient with keratoconus or other corneal disorders can have the procedure. In the study by Hashemi and colleagues, the researchers limited their patients to those with more than 400 microns of corneal tissue. It is suspected that without ample corneal tissue, the UV-A light from the CXL device could damage corneal endothelial cells. Other similar exclusion criteria in the studies revolved around previous eye surgery and evidence of corneal scarring prior to surgery. While CXL complications are rare, the Witting–Silva group did report three adverse events over the three year period. However, all events were temporary and were resolved.

The two studies discussed here are among several that highlight the safety and benefits of CXL in treating keratoconus. While the FDA has reviewed applications for approval of this treatment, CXL is not yet officially recognized among most health systems in the US, including the military. The anticipation is that in the long-term, CXL may become available to military personnel as an alternative to traditional treatment options, such as contact lenses and corneal surgery. Because this disease has direct implications for force readiness and is a potentially career-changing diagnosis for Service members, the Department of Defense continues to monitor CXL as a treatment for keratoconus. Active duty personnel should discuss this diagnosis and available treatment options with their medical provider and commanding officer for further guidance.

Conclusion.
This production was brought to you by the Vision Center of Excellence. Our mission is to lead and advocate for programs and initiatives to improve vision health, optimize readiness and enhance quality of life for Service members and Veterans. Working with TRICARE, the Military Health System, other Centers of Excellence and the Veterans Health Administration, the Vision Center of Excellence works to enhance collaboration between Department of Defense and Department of Veterans Affairs vision care providers, provide guidance for clinical practice and facilitate patient-centered support. For more information, visit us online at vce.health.mil or on Facebook.

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APPENDIX

A: Phonetic Guide.

Phonetic Guide		
1	Hashemi	Ha-sh-eh-mee
2	Wittig	ViT-tig
3	Keratoconus	Kair-a-T'-cone-us