Периферический кросслинкинг роговичного коллагена (П-КРК) ультратонких роговиц в терминальных стадиях кератоконуса: новая техника
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Кросслинкинг роговичного коллагена (КРК) направлен на предотвращение прогрессирования кератоконуса и широко признан в качестве "золотого стандарта" в лечении этого заболевания. Однако у пациентов с толщиной роговицы менее 400 мкм стандартный кросслинкинг противопоказан. Это заставляет офтальмохирургов прибегать к методике трансэпителиального КРК, которая считается менее эффективной. В данной работе описан альтернативный подход к пациентам с ультратонкой роговицей и далеко зашедшим кератоконусом — периферический КРК (П-КРК), при котором дезэпителилизация производится, но не затрагивает центр роговицы. Новая методика также включает в себя использование гипоосмолярного раствора рибофлавина. Представлен случай выполнения П-КРК у пациента с крайне далеко зашедшим кератоконусом IV стадии. Наименьшая толщина роговицы до операции составляла 215 мкм, максимальное значение кератометрии (Kmax) — 88,1 дптр, астигматизм — 11,2 дптр. Через 4 мес после П-КРК наименьшая толщина роговицы увеличилась на 42 мкм, Kmax снизился на 1,4 дптр, а астигматизм уменьшился на 3,2 дптр.

Ключевые слова: кросслинкинг коллагена роговицы, ультратонкая роговица, кератоконус.

Peripheral corneal cross-linking (P-CXL) for ultrathin corneas with severe keratoconus: a new technique
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Corneal cross-linking (CXL) is aimed at halting the progression of keratoconus and is widely considered to be the golden standard in its treatment. It is usually contraindicated, however, in patients with corneal thickness of less than 400 µm, leaving the ophthalmic surgeon no alternative but to perform transepithelial CXL (epi-on), usually regarded as less effective. We report a novel approach for ultrathin corneas with severe keratoconus — peripheral corneal cross-linking (P-CXL), in which corneal epithelium is still removed but the apex of the cornea is left untouched. Hypo-osmolar riboflavin solution is used as well. P-CXL was performed on a remarkably developed stage IV keratoconus with the thinnest pachymetry of 215 µm, Kmax of 88.1 D and astigmatism of 11.2 D. Four months after P-CXL, the thinnest pachymetry increased by 42 µm, Kmax decreased by 1.4 D, and astigmatism also decreased by 3.2 D.

Keywords: corneal collagen cross-linking, ultrathin cornea, keratoconus.

Keratoconus (KC) is a bilateral non-inflammatory corneal ectasia that usually develops in the second decade of life and is characterized by a gradual loss of thickness and subsequent conical deformation of the cornea [1]. This leads to irregular astigmatism and a decrease in visual acuity. In 20 to 25% of cases, corneal transplantation may be required.

Conservative surgery, aimed at improving vision and/or halting the ectasia in its early stages, include corneal collagen cross-linking (CXL) [2], mini asymmetric radial keratotomy (MARK) [3], circular keratotomy (CK) [4], and implantation of intrastromal corneal ring segments (ICRS) [5]. CXL, the most recent among these, is now widely regarded as the most effective treatment for progressive keratoconus as it directly addresses the intrinsic structural weakness of the cornea by reinforcing the stroma and, thus, stopping the evolution of KC.

The standard protocol of CXL (‘epi-off’, or the ‘Dresden Protocol’), however, is contraindicated in patients with less than 400 µm of corneal thickness, leaving surgeons no alternative but to perform transepithelial CXL (‘epi-on’), a technique that gives less discomfort to the patient but is also generally regarded as less effective, especially when dealing with aggressive forms of KC [6]. We have, therefore, developed a novel approach to severe keratoconus of ultrathin corneas, a condition that requires surgical intervention of the highest effectiveness. Peripheral corneal cross-linking (P-CXL) also involves...
epithelium removal, but, unlike the epi-off technique, leaves a small island of untouched epithelium on the thinnest part of the cornea identified in advance by tomographic examination.

**Case report**

In September 2015, a 55-year-old man presented with progressive bilateral KC diagnosed 30 years before. Even in his contact lenses the patient complained of very poor vision from his left eye, which was, indeed, in a considerably worse condition than the right one. The patient underwent a thorough clinical examination, including measurement of uncorrected (UCVA) and best corrected visual acuity (BCVA), corneal tomography, corneal topography, axial biometry, pachymetry, endothelial cell count, keratometry, and slit lamp examination. Left eye results were the following: BCVA 1.69 logMAR (20/1000, legal blindness), Kmax 88.1 D, Kmed 75.5 D, thinnest pachymetry 215 µm, and 11.2 D of astigmatism (Fig. 1).

With the aim of avoiding penetrating keratoplasty (PKP), a procedure the patient had been told elsewhere he had to undergo, we decided to perform a conservative intervention using the modified technique of peripheral corneal cross-linking (P-CXL). A written informed consent was obtained as a part of our pre-operative routine. Topical anesthesia with 0.4% benoxinate chloride was applied prior to surgery and the eyelids were kept open using surgical forceps. Corneal epithelium was removed with an ophthalmic scalpel (MicroFeather; Feather Safety Razor Co., Ltd., Osaka, Japan) under a surgical microscope, at that, a small island of epithelium on the thinnest part of the cornea, identified in advance, was left untouched (Fig. 2).

Iso-osmolar riboflavin solution was applied 10 times at 3-minute intervals 30 minutes before UV-A irradiation, following which hypo-osmolar riboflavin solution was also applied for 5 minutes every 20 seconds, thus, temporarily increasing corneal thickness. Moreover, iso-osmolar riboflavin was applied 6 times at 5-minute intervals during the 30-minute UV-A exposure (UV-X illumination system version 1000, IROC AG, Switzerland). Immediately after CXL, we inserted a bandage contact lens and prescribed topical antibiotics and non-steroidal anti-inflammatory drops.

**Results**

Four-and-a-half months after peripheral corneal cross-linking, the set of examinations was repeated, revealing a strong improvement in terms of both corneal regularity and corneal thickness (Fig. 3). Results were the following: Kmax 86.7 D, Kmed 70 D, thinnest pachymetry 257 µm, and 8 D of astigmatism. BCVA greatly increased, reaching 0.69 logMAR (20/100) (see Table). No postoperative complications were noted.

**Discussion**

Today we are witnessing high availability of more accurate instruments for detection of keratoconus and an
increasing awareness of it among the general public — a situation that has resulted in a growing number of patients diagnosed with KC. We face, however, the challenge of properly treating patients with corneal thickness of less than 400 microns.

There is also an ongoing debate on the validity of transepithelial corneal cross-linking, a technique that gives less discomfort to the patient, but is also generally regarded as less effective [6]. The latter has been confirmed in the treatment of pediatric patients with KC [7, 8]. We have been performing CXL since 2005 and our experience brought us to the same conclusion. Therefore, a novel approach has been developed, the one that enables effective treatment of patients with ultrathin corneas without running the risk of keratoconus progression after transepithelial CXL.

Peripheral corneal cross-linking (P-CXL) is the latest CXL modification intended to serve as an alternative to transepithelial CXL in patients that are normally rejected from the standard protocol. Other modified CXL protocols include accelerated corneal cross-linking [9], pocket corneal cross-linking [10], contact lens-assisted collagen cross-linking (CACXL) [11], and CXL with partial epithelial removal [12]. All of them have proved promising, and there is thus no need to perform the currently common “epi-on” procedure.

In our case, peripheral corneal cross-linking was successful in treating an extremely developed stage IV keratoconus with Kmax of 88.1 D and thinnest pachymetry of 215 µm, eliminating the need for penetrating keratoplasty. Obviously, there should be more patients treated with P-CXL and followed up for long enough periodism before one can discuss the generalizability of the findings presented in this case report. We encourage fellow ophthalmic surgeons to choose conservative and still effective treatments whenever possible, especially when dealing with very developed keratoconus or very young patients, considering that such treatments may help avoid corneal transplantation and subsequent refractive surgery [13].

None declared.