

CLINICAL STUDY, ONE YEAR AFTER THE CORNEAL COLLAGEN CROSS-LINKING PERFORMED FOR THE PATIENTS WITH KERATOCONUS

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Abstract: The aim of this work is to present retrospective results obtained after corneal collagen cross-linking procedure for the patients with progressive keratoconus. **Materials:** This study included patients with progressive keratoconus in stage II and III, aged between 16 and 44 years old. **Methods:** The therapeutic procedure has been applied to 49 patients (71 eyes); corrected and uncorrected visual acuity, corneal thickness values and topographic aspects were recorded before and after surgery at 1, 3, 6 and 12 months. **Results:** Visual acuity remained unchanged for the majority of cases, and for 36 cases it improved with 1-4 Snellen lines. The average increase of the corneal thickness was 10.01 ± 7.03 microns. The average reduction of the maximum keratometric readings was 1.20 ± 1.05 dioptres. **Conclusions:** Stable visual acuity, the increase of the corneal thickness and the decrease of the maximum keratometric readings show that this technique represents a method to stop the progression of keratoconus.

Keywords: progressive keratoconus, corneal collagen cross-linking, pachimetry, keratometry

Rezumat: Scopul lucrării este de a prezenta rezultatele retrospective obținute după efectuarea corneal collagen cross-linking la pacienți cu keratoconus progresiv. **Material:** Studiul cuprinde pacienți cu keratoconus progresiv, stadiul II, III, cu vârsta cuprinsă între 16 și 44 de ani. **Metoda:** Procedura terapeutică a fost aplicată la 49 de pacienți (71 de ochi), acuitatea vizuală necorectată și corectată, valorile pachimetrice și aspectele topografice au fost înregistrate pre- și post-operator la 1, 3, 6 și 12 luni. **Rezultate:** Acuitatea vizuală a rămas nemodificată la majoritatea cazurilor, iar la 36 de cazuri s-a îmbunătățit cu 1-4 linii Snellen. Media de creștere a valorilor pachimetrice a fost de 10.01 ± 7.03 microni. Media de reducere a valorii maxime keratometrice a fost de $1.20 D \pm 1.05 D$. **Concluzii:** Acuitatea vizuală stabilă, creșterea grosimii corneene și diminuarea valorii maxime keratometrice indică faptul că tehnica utilizată reprezintă o metoda de stopare a progresiei keratoconusului.

Cuvinte cheie: keratoconus progresiv, corneal collagen cross-linking, pachimetrie, keratometrie

characterized by conical ectasia and central and paracentral thinning due to corneal structure alterations. It starts usually in teenagers, having a progressive evolution with the reduction of visual acuity (VA) through irregular astigmatism determined by corneal ectasia. It is considered that disease progress in the moment of reduced VA, decreasing of the corneal thickness with 20 microns and increasing of the maximum keratometric value (Kmax) with one diopter (D).

The cause of this disease still remains a mystery. Laboratory research performed at the corneal level of the patients with keratoconus indicates an imbalance between proteinase enzymes and their inhibitors (in the sense of the increasing of the activity of the proteinase enzymes and of the decreasing of the activity of the proteinase enzyme inhibitors) having as effect the destruction of the structural proteins and of their bonds, shaping the thinning and the reduction of the mechanical corneal stiffness. The cause of the increasing of the proteinase activity for the patients with keratoconus is unknown.

Cornea is responsible for ultraviolet light absorption which enters the eye and the release of the oxygen free radicals under these actions. Oxygen free radicals are high energy molecules which affect corneal cells by acting upon proteins, DNA and cell membrane. At healthy persons the removal of oxygen free radicals is performed by antioxidant proteins, but in the cornea of the patients with keratoconus is noticed a deficiency of antioxidant enzymes which affects the cells and release proteinase enzymes.

Cross-linking represents the natural or induced reaction of biochemical, enzymatic or photodynamic polymerization of collagen, characterized by the formation of intra- and inter-helicoidally links, in order to increase the tissue stiffness.

Corneal collagen cross-linking (C3R) induced by topical treatment with riboflavin and exposure of ultraviolet light of A type stand for photopolymerization of stromal collagen fibres, opposing the evolution of the corneal ectasia, by increasing its strength. Beside the strength and the bio-mechanic stability increasing, through corneal collagen cross-linking is also obtained an increase in the diameter of the collagen fibres, anticholagenazic effect, stimulation of the keratocytes apoptosis and their repopulation from deep stroma.

INTRODUCTION

Keratoconus is a corneal bilateral non-inflammatory disease with asymmetric evolution,

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PURPOSE OF THE STUDY

The aim of this study is to evaluate the functional pachymetric and topographical results obtained after 1 year from corneal collagen cross-linking intervention for the patients with keratoconus.

MATERIAL AND METHOD

Materials: this study includes patients with progressive keratoconus, with ages after 16 years old, clear cornea without opacities and corneal thickness bigger than 400 microns. It has been excluded patients with previous corneal surgical intervention, aphakia, pregnancy, autoimmune diseases. It was measured pre- and post-intervention, for all patients, the refraction, visual acuity with and without correction, the thickness of the cornea measured by ultrasonic pachymetry, intraocular pressure, and topographic aspects were recorded. Similarly, slitlamp biomicroscopy and ophthalmoscopy have been performed. Post-surgery checks were performed in the first and third day, and at 1, 3, 6 and 12 months.

Method: the same intervention technique has been applied to all patients in aseptic conditions under topical anaesthesia with lidocaine 4%, instilled 3 times in 15 minutes. After lid speculum application, corneal desepithelization has been done on a surface of 9 mm, followed by riboflavin 0.1% in dextran 20% instillation, at every 3 minutes, for 30 minutes. The corneal impregnation with riboflavin is checked using blue filter.

Exposure to type A ultraviolet light for 30 minutes using a lengthwise of 370 nm and 3 mW/cm² at a distance of 5 cm from the corneal apex, the instillation of riboflavin continue during this period of time at every 5 minutes. After treatment, the washing of the corneal surface has been performed and the therapeutic lens has been applied. As post-surgery medication, antibiotics and artificial eye-drops were used till the corneal epithelization, and after that corticosteroids were topically administrated for two weeks.

Results. C3R was applied to 49 patients (71 eyes), for 22 patients the method being used for both eyes. Between these, 29 were males and 20 females. The age of the patients was between 16 and 44 years old.

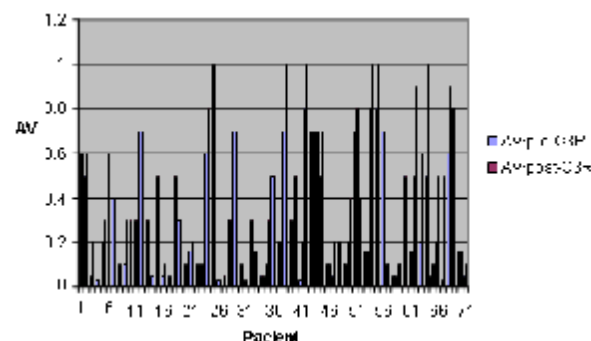
The therapeutic procedure has been applied to 24 cases with a Kmax value smaller than 48 D; 30 cases have Kmax between 48 and 53 D and 17 cases with Kmax higher than 54 D.

The VA without correction remained constant for 31 patients after C3R performance, for the remaining patients the VA increasing with 1-4 Snellen lines (SL). For 9 cases VA has improved with 1 SL, for 22 cases with 2 SL, for 5 cases with 3 SL and for 4 cases with 4 SL. For 6 cases after the therapy VA improved to the value of 20/20. Figure 1 shows the evolution of the VA without corrections after C3R.

The best visual acuity was obtained for the majority of the pre- and -post surgery patients by using hard contact lenses. The use of contact lenses was interrupted 2 weeks before C3R. After surgery the lenses

were carried after 4 weeks. For 12 patients it was necessarily the change of the contact lenses parameters, in the direction of increasing the curvature radius and of reduce the dioptres 5 patients improved their visual acuity by wearing spectacles. For 6 patients it was not necessarily the correction of the visual acuity after collagen corneal cross-linking.

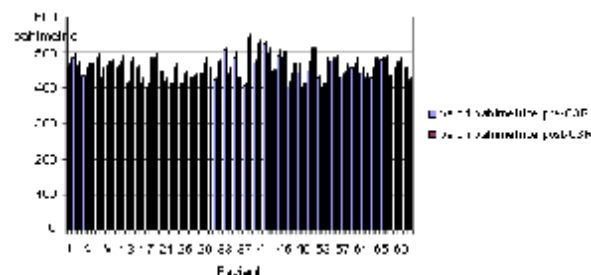
Picture no. 1. Visual acuity without correction before and after C3R



Intraocular pressure has been maintained in normal limits.

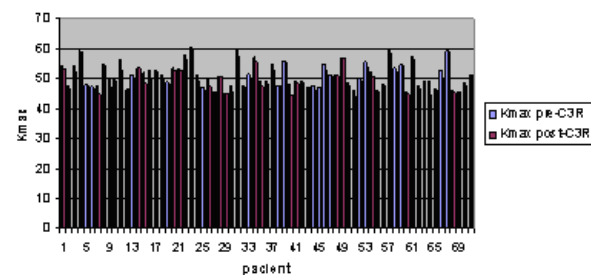
The variation of the average pachymetric values was 10.01 microns, with a standard deviation (SD) of ± 7.03 (455.25 \pm 31.86- 465.25 \pm 32.25), correlation coefficient (R) 0.97 (picture no. 2).

Picture no. 2. Evolution of the pachymetric values before and after C3R



Regarding the maximal keratometric values, it has been obtained a reduction of the values by 1.20 \pm 1.05 (51.15 \pm 4.09 – 49.95 \pm 4.16), R = 0.96, SD = 1.05 (figura 3).

Picture no. 3. Evolution of Kmax values before and after C3R



After surgery some patients have a slight discomfort in the first day, re-epithelization has been

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produced in 3-4 days without any other complications showed in literature (haze, infiltrations or corneal infections). The intraocular pressure, the number and the morphology of the endothelial cells remains unchanged.

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DISCUSSION

The mechanism of the increasing of the biomechanical stability of the cornea is represented by the formation of the covalent bonds after adding riboflavin (photo-sensitive agent) on the cornea after epithelium was removed and exposure to A type ultraviolet light. The free radicals formed interacts with aminoacids at the collagen molecules level forming and enforcing new covalent bonds, the photo-polymerization process being initiated by oxidative deamination. During the intervention the UVA absorption at the cornea level is enhanced by riboflavine application, and without this lesion of the lens and the retina may occurs. The removal of the corneal epithelium enhances the absorption of this macromolecule at the cornea level.

Our results demonstrate that this therapeutic procedure stops the progression and even determine in some cases a regression of the corneal ectasia. The reduction of Kmax values and the improving of VA is probably the results the increased stability and of the shrinking of the length of collagen layer. Caporossi in its study make the hypothesis that the improved VA is determined by corneal regularization, but its cause remains unclear. In our study the reduction of the Kmax value is 1.2 D, smaller than the reported one (2 D).

Pachymetric changes similar with those from literature are determined by the corneal hydration degree through the hydrophilic capacity of stroma proteoglicans (dermatan and keratan-sulphat).

CONCLUSIONS

Stabile VA, sometime improved, increasing of the corneal thickness and decreasing of the Kmax values showed that this therapeutic procedure is sure, easy to perform it, and stops the progression of the disease

Corneal collagen cross-linking with riboflavine and UVA is a minimum invasive procedure which do not obstruct the following penetrate or lamellar keratoplasty if necessarily.

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