CORNEAL COLLAGEN CROSS-LINKING, INTRASTROMAL CORNEAL RING, PHOTO KERATECTOMY WITH EXCIMER LASER-THERAPEUTIC PROCEDURES FOR KERATOCONUS

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Abstract: This work presents certain theoretical aspects of the therapeutic procedures used in keratoconus with the aim of stabilizing the evolution of the disease and improving their quality of life

Keywords: corneal collagen cross-linking, intrastromal corneal ring, photokeratectomy laser excimer

Rezumat: Lucrarea prezintă aspecte teoretice ale procedeelor terapeutice folosite în keratoconus în scopul stabilizării evoluției afecțiunii și al îmbunătățirii calității vieții acestor pacienți.

Cuvinte cheie: corneal collagen cross-linking, inele corneene intrastromale, fotokeratectomie laser excime

In the last years the research permitted the development and the applications of new therapeutic procedures in aim to stop the keratoconus evolution, to correct the visual acuity and to reduce the necessity of lamellar or perforate keratoplasty.

Keratoconus is a non-inflammatory corneal dystrophy, with asymmetric, progressive, and bilateral evolution, characterized by central or paracentral corneal thinning and conical ectasia.

The progress of the corneal ectasia vary from one patients to another, the chance of evolution seems to be higher in the cases with an early start, after 30 years old is registered a slowing of evolution, probably caused by naturally cross-linking of collagen fibres. It is considered that the disease progressed in the moment of the visual acuity decrease, by myopia and irregular myopic astigmatism, the reduction of the corneal thickness and in the increase of keratometric values with one dioptre, at repeated checks made at 3-6 months. Function of the change of these parameters, it is decided the application of different therapeutic methods.

A better visual acuity can be obtained with rigid contact lenses, at the incipient stadium, as well as in advanced ones; in the case of the intolerance in wearing of these contact lenses, intrastromal corneal ring implant may be considered for visual correction. Corneal collagen cross-linking is performed only for an advanced disease, even in the situation of a better visual acuity obtained by using hard contact lenses or if the progress of keratoconus is noticed.

Corneal collagen cross-linking with riboflavine

and UVA is a new method to stabilize patients with keratoconus and corneal ectasia, the original idea belonging to Dr. Theo Seiler, which utilizes for the first time riboflavine and type A ultraviolet for the photopolymerization of the collagen fibers with the aim of stiffing the cornea by creating covalent bonds between collagen molecules at their level (intra- and interhelycoidal bonds), the principle of the method being already applied in dental medicine and orthopedy. Initially, Seiler has establish the parameters to be used: riboflavine concentration, UVA length wave, time, profoundness of action, the efficiency of the measurements by extensiometry, the first study regarding the efficiency of cross-linking in the treatment of keratoconus being published in 1998.

The irradiation of the riboflavine with UVA affects the chemical internal equilibrium, producing free oxygen radicals. At that moment the riboflavine molecules are unstable, becoming stable in the moment of bonding at two collagen fibres, phenomenon that is the base of cross-linking. The photopolymerization process is initiated by oxidative deamination and is followed by the formation of bonds between collagen fibres.

The effects of the cross-linking are not instantaneous, beside the influence of the bio-mechanical stability of the cornea, cross-linking induces an increase of the diameter of the collagen fibres, anticholagenazic effect and the stimulation of the keratocytes apoptosis. Ultrastructure studies showed that only after one month an increase of stromal density is produced, the regeneration of nerves fibers, keratocytes activation from to deep of the stroma and from periphery. After 3 months start the repopulation of keratocytes and the increase of the density of extra cellular matriceal fibers. In published studies the reduction of the keratometric values with 2 D and the increase of the corneal thickness with 10-15 microns, an increase of the visual acuity with 2 Snellen lines were generally obtained after 18-24 months from intervention.

The intervention is performed under topic anaesthesia. After corneal epithelium was removal on 9 mm surface, riboflavine izo-osmolar 0.1% in dextran T500 20% is instilled at every 3 minutes for 30 minutes. The diffusion is verified by the visualization of the riboflavin in anterior chamber at slit lamp examination. Also is measured the thickness of the cornea by ultrasonic pahimetry. If at the pahimetry the corneal thickness is smaller than 400 microns, riboflavin 0.1% hypo-osmolar (obtained by dilution with physiological ser, sodium chloride 0.9% 310 mOsm/L) at every 20 seconds for 5 minutes and pahimetry is repeated again. After that, the cornea is irradiated with UVA 370 nm, 3mW/cm2, from a distance of 5 cm from the corneal apex. Finally, after corneal washing a soft contact lens is applied together with antibiotics and artificial eye drops till the epithelium is regenerate. Two weeks after the surgery corticosteroid is administrated topically.

The method is applied for patients with incipient keratoconus, progressive, with ages between 16 and 45 years old, clear cornea and the thickness of the cornea higher than 400 microns. The method is not used in aphakia, previous corneal surgical intervention, corneal thickness under 400 microns, numbers of endothelial cells under 2000, pregnancy, auto-immune diseases, herpes keratitis.

Pre- and post-surgery is necessary the monitoring of the visual acuity, corrected and uncorrected, refraction, keratometric and pahymetric values, topographical aspects. In order to supervise the possible adverse effects after the intervention, slit lamp examination and ophthalmoscopy are performed, as well as intraocular pressure. The number of endothelial cells is also measured.

Intrastromal corneal ring represent an alternative treatment for keratoconus which do not stop the evolution, increase the uncorrected and corrected visual acuity, the tolerance at contact lenses and the use of spectacles, delaying the necessity of corneal transplant, being easy to be removed. Intrastromal corneal ring flattening the corneal centre, decrease the myopia and astigmatism and let the optical correction. In present are used two types of intrastromal corneal ring: Ferrara and Intacs, function as corneal ectasia type: classical situated in the bottom half or central. In classical ectasia an Intacs ring is implated, and in the central one two Ferrara rings. Generally, as the optical zone is smaller the visual effect is better, but a smaller optical zone is associated with a lower quality of the vision, due to the formation of glare and haze.

Technique: Under topical anaesthesia, a radial incision of 1 mm is performed till 70% profoundness in the cornea and with a special dissector 2 channels (superior and inferior) are performed, and the rings are inserted at their level.

The procedure may be applied for:

- patients with keratoconus with intolerance at hard contact lenses (glare, haze, diplopia, associated or not with pain, discomfort, tearing, recurrent erosions),
- clear cornea and thickness bigger than 450 microns,
- VA better than 20/50.
- keratometric average value in the cornea centre smaller than 55D.

The procedure is not indicated for central corneal opacities, inadequate pahimetry values, previous ocular

interventions, herpes keratitis, conjunctive tissue problems.

Possible complications:

- periferic corneal haze at the intrastromal tunnel level which usually appears immediately after surgery, due to mechanical separation of the cornea lamella through surgery procedure
- sediments at the level of the intrastromal channels at 2 months after intervention
- gelatin opacities which usually appears at 8 months after intervention
- iron epithelial deposits appearing in the inferior half, next to internal edge of the ring due to the evaporation of the tear film, which induce an increasing in the concentration of iron and so the accumulation of iron in epithelial cells and the reduction of the superficial cells turnover in this zone
 ejection and migration of rings

Photokeratometry laser excimer (PRK) topographically guided is used so far experimentally for the rehabilitation of visual acuity of patients with keratoconus in some medical canters, but, by the ablation realized a destabilization of cornea is induced and their thinning, followed possibly by progression. For this reason, the latest trends are to utilize this technique simultaneously with C3-R. Theoretically the ablation restore the form of the corneal surface and C3-R should stop the progress of the disease. Thus, by this method it is possible to correct both spherical component and 75% from astigmatism, the ablation do not exceed 50 microns. and optical zone 5 mm minimum. The technique is applied in the cases in which the pre-surgery corneal thickness exceeds 450 microns.

The performance of PRK topographically guided at 6 months- 1 year post C3-R would be influenced by the next limits:

- cross-linked cornea is removed by PRK thus diminishing the C3-R benefits
- ablation corneal rate after C3-R may differ from the ablation on cornea without C3-R
- higher haze incidence because after 6 months after C3R a repopulation with new keratocites is produced.

It seems that C3-R performed on ablationated stroma offers the advantage of keratocites depopulation and reduces the possibility of haze apparition.

Long term results of these association are not fully known but all these research are made in the aim of avoiding keratoplasty, to which complications are well known. From all these procedures, C3-R is easy to be performed, non-invasive, cheap and its use may be carried together with the other methods for a better recovery of visual acuity.

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