Contact Lens & Anterior Eye 37 (2014) 438–441

Contents lists available at ScienceDirect

Contact Lens & Anterior Eye

journal homepage: www.elsevier.com/locate/clae

Trans epithelial corneal collagen crosslinking for progressive keratoconus: 6 months follow up

Maddalena De Bernardo[a], Luigi Capasso[b], Antonia Tortori[b], Michele Lanza[c], Luisa Caliendo[a], Nicola Rosa[a,*]

[a] Department of Medicine and Surgery, University of Salerno, Salerno, Italy
[b] U.O.C. Prelievo e Trapianto Cornee, Pellegrini Hospital, Naples, Italy
[c] 2nd University of Naples, Naples, Italy

ARTICLE INFO

Article history:
Received 7 September 2013
Received in revised form 25 June 2014
Accepted 21 July 2014

Keywords:
Keratoconus
Cross linking
Corneal elasticity
Corneal thickness
Axial length

ABSTRACT

Purpose: To evaluate keratoconus biomechanical changes after transepithelial corneal collagen cross linking (TE CXL) using riboflavin and ultraviolet A (UVA).
Setting: Second University of Naples, Naples, Italy.
Design: Prospective non comparative case series study.
Methods: Patients with progressive keratoconus were examined, before and during a 6 months follow up after TE CXL, with a Pentacam, an Ocular Response Analyzer and an IOLMaster.

Best corrected visual acuity (BCVA), refraction, corneal thinnest point (CTP), keratometry readings at the keratoconus apex (K_{max}), axial eye length (AL), corneal volume (CV) anterior chamber volume (ACV), anterior chamber depth (ACD), corneal hysteresis (CH) and corneal resistance factor (CRF) were evaluated.
Results: Thirty-six eyes of 36 patients with progressive keratoconus were analyzed. Six months after treatment there was a significant improvement in BCVA ($p < 0.01$), no significant changes in refraction ($p = 0.57$), CTP ($p = 0.07$), K_{max} ($p = 0.88$), AL ($p = 0.07$), CV ($p = 0.38$), ACV ($p = 0.07$), ACD ($p = 0.7$), CH ($p = 0.1$) and CRF ($p = 0.3$).
Conclusions: According to our results TE CXL stabilizes most of the patients with progressive keratoconus, without affecting in negative way the corneal elasticity.

Keratoconus is a corneal ectasia resulting from non inflammatory, progressive thinning of the corneal stroma [1]. Its initial management is based on refractive correction with spectacles and contact lenses or corneal rings. Further ectatic progression may lead to corneal transplantation in 10–20% of patients [2].

In 2003, Wollensak et al. [3,4] to halt the natural progression of keratoconus introduced corneal collagen crosslinking (CXL) using riboflavin and ultraviolet-A (UVA).

This procedure is proved to be effective in increasing corneal stiffness [3,5] and consequently giving a stabilization of keratoconus, in some cases improving the refractive and topographic features [6–8].

Recently, Boxer Wachler et al. [9] suggested a modification of the technique by keeping the epithelium intact, named epithelium-on or transepithelial CXL (TE CXL). This is made possible by the use of enhancers, such as trometamol and sodium ethylenediaminetetraacetic acid (EDTA), that help riboflavin, an hydrophilic macromolecule, to penetrate the corneal stroma through an intact epithelium, thereby avoiding the need for epithelial debridement [9].

This study aims to evaluate the efficacy and safety of the TE CXL in the treatment of patients with progressive keratoconus.

1. Methods

Patients with a progressive keratoconus, documented by refraction and corneal topography in the last 6 months were evaluated in prospective, non-randomized study. Patients with history of previous corneal surgery, systemic autoimmune disease, diabetes, evidence of severe dry eye, corneal scars and corneal thickness less than 380 μm were excluded from the study. After the nature and intent of the study had been fully explained, a written informed consent from each subject was obtained. The study protocol was consistent with the tenets of the Declaration of Helsinki and

* Corresponding author at: Department of Medicine and Surgery, University of Salerno, via Salvatore Allende1, Baronissi, Salerno, Italy. Tel.: +39 089965063; fax: +39 0817642360.
E-mail address: nrosa@unisa.it (N. Rosa).

http://dx.doi.org/10.1016/j.clae.2014.07.007
1367-0484/

Table 1
Best corrected visual acuity (BCVA), spherical equivalent (Sph eq) and cylinder (Cyl), corneal thinnest point (CTP), keratometry readings at the keratoconus apex (K max), axial eye length (AL), corneal volume (CV) anterior chamber volume (ACV) and depth (ACD), corneal hysteresis (CH) and corneal resistance factor (CRF) before treatment and at the 6 months follow up (mean ± standard deviation, and range).

	Pre op Mean ± sd	Range	6months Mean ± sd	Range	*P*
BCVA	0.72 ± 0.23	0.35 to 1	0.89 ± 0.28	0.4 to 1.4	< 0.01
Sph eq (D)	−2.06 ± 3.03	−13.25 to +1.88	−1.80 ± 2.72	−9 to +2.25	0.57
Cyl (D)	−2.76 ± 1.34	−6 to −0.75	−2.78 ± 1.39	−6 to 0	0.55
CTP (μm)	467.5 ± 41.1	380 to 549	459.8 ± 47.24	339 to 535	0.07
K max (D)	55.43 ± 5.4	48.1 to 68	55.48 ± 4.8	48.6 to 66.2	0.88
AL (mm)	23.54 ± 0.9	22.16 to 24.93	23.56 ± 0.92	22.16 to 24.99	0.07
CV (mm^3)	58.15 ± 3.3	52.30 to 66.40	57.82 ± 3.4	51.30 to 65.70	0.38
ACV (mm^3)	213.9 ± 24.8	168 to 253	216.9 ± 24.8	176 to 267	0.07
ACD (mm)	3.42 ± 0.3	2.87 to 3.89	3.42 ± 0.29	2.86 to 3.91	0.7
CH (mmHg)	8.3 ± 1	6.9 to10.3	7.9 ± 1.2	6.4 to 10.2	0.1
CRF (mmHg)	6.7 ± 1.4	4.3 to 9.3	6.4 ± 1.6	4.2 to 9.4	0.3

received the IRB approval. All patients had a complete preoperative ophthalmologic examination including measurement of best-corrected visual acuity (BCVA), slit lamp and fundus examination, corneal evaluation by a Scheimpflug imaging device (Oculus Pentacam, Optikgerate GmbH, Wetzlar, Germany), measurement of the axial length (AL) with an IOLMaster (Carl Zeiss Meditec, Jena, Germany), evaluation of the biomechanical properties of the cornea: corneal hysteresis (CH) and corneal resistance factor (CRF), with an Ocular Response Analyzer (Reichert Technologies, Depew, USA).

All the patients were treated with UVA–riboflavin CXL under aseptic conditions using topical preoperative anesthesia with oxybuprocaine hydrochloride 0.4% eye drops. Before the procedure, 2% pilocarpine eye drops were instilled in the eye to be treated. Each patient was draped, the ocular surface rinsed with balanced saline solution (BSS), a lid speculum inserted. A ring-shaped silicone container (Sooft, Montegiorgio, Italy) was placed on the cornea and used to improve riboflavin penetration. To allow sufficient saturation of the stroma, Riboflavin 0.1% in 15% dextran solution supplemented with tris-hydroxymethyl aminomethane and sodium EDTA (Ricrolin TE, Sooft, Montegiorgio, Italy) was applied to the cornea, in the silicone ring, 30 min before the irradiation, every 5 min. A calibrated UV power meter (UV LIGHT meter model yk-34uv, Lutron electronic, Coopersburg, USA) was used to control the desired levels of irradiance before each treatment. After that, an 8.0 mm diameter of the central cornea was irradiated with the Vega C.B.M. X-linker (C.S.O. Firenze) using standard parameters (UVA 365 nm, 3 mW/cm^2). During the 30 min irradiation, drops of riboflavin solution were applied to the cornea every 2–3 min to maintain the necessary concentration of riboflavin and to prevent corneal drying. The centration of the treatment was controlled by the surgeon. After treatment, the eye surface was washed with BSS, and patients received ofloxacin 3 mg/ml eye drops four times daily for one week.

Statistical analysis was performed using the paired Student *T* test. $P < 0.01$ was considered to be statistically significant.

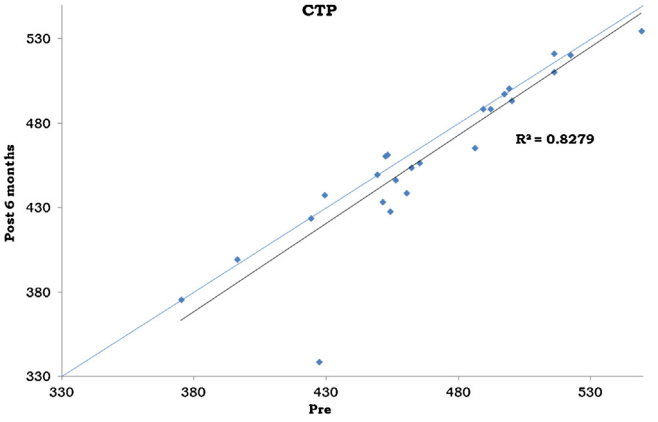

Fig. 1. Correlation between corneal thinnest point (CTP) measured before and 6 months after trans epithelial cross linking.

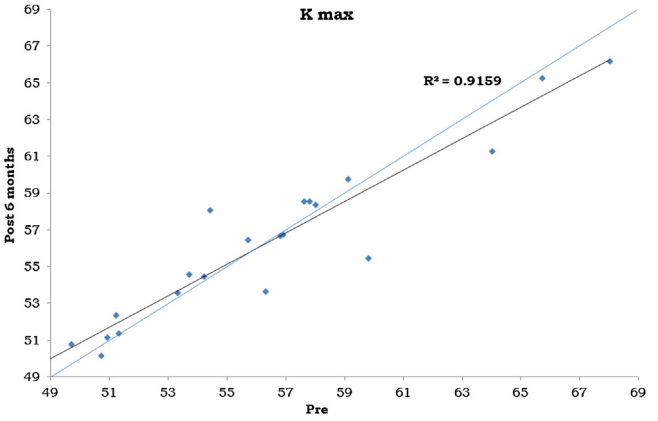

Fig. 2. Correlation between keratometry readings at the keratoconus apex (K_{max}) measured before and 6 months after trans epithelial cross linking.

2. Results

Thirty-six eyes of 36 patients (28 men) with a mean age of 24.5 ± 5 years (range from 12 to 33) with a progressive keratoconus, documented by refraction and corneal topography in the last 6 months were included in the study. Six months after the procedure, we observed a statistically significant improvement in BCVA and no significant changes in refraction (in terms of spherical equivalent and cylinder values), corneal thinnest point (CTP), keratometry readings at the keratoconus apex (K_{max}), AL, corneal volume (CV), anterior chamber volume (ACV), anterior chamber depth (ACD), CH and CRF, compared to the preoperative data, as shown in Table 1 and Figs. 1–8.

3. Discussion

Several studies have been published reporting the clinical data after TE CXL, but to the best of our knowledge, none of them evaluated anterior segment and corneal biomechanical changes.

Leccisotti et al. [10] in 51 eyes of 51 adult patients found an improvement in mean BCVA, a reduction in mean manifest spherical equivalent refraction, that were both statistically significant ($P < .05$) whereas there was a not significant change in mean average