Safety in Corneal Refractive Therapy for myopia control

Laura Batres[1] PhD; Julia Bodas[1] Msc; Gonzalo Carracedo G[2] OD, PhD

[1] Department of Optometry and Vision, Faculty of Optic and Optometry, Universidad omplutense de Madrid, Madrid, Spain

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Corresponding Author:

Gonzalo Carracedo Rodríguez
Faculty of Optic and Optometry
Department Optometry and Vision
C/Arcos del Jalon 118
28032 (Madrid)
Spain
e-mail: jgcarrac@ucm.es

INTRODUCTION

Orthokeratology is a clinical technique that uses specially designed and fitted contact lenses to reshape the cornea temporarily for modifying or avoiding the patient refractive error. The main clinical application of orthokeratology is the reduction of myopia through flattening the center of the cornea and steepening the periphery, although there are lens designs for other refractive errors as an astigmatism, hyperopia and presbyopia(1).

In the last years orthokeratology has been proposed as a treatment for myopia progression. It has been established that the corneal changes provoked by orthokeratology lenses modify the peripheral refraction, from hyperopic to myopic peripheral refraction(2). The role of peripheral refraction in the axial length progression control has been described in several studies(3-6). The corneal topographic changes induced by orthokeratology lens wearing have been reported in several studies(7, 8). A successful orthokeratology treatment makes a central flattened zone named treatment zone and a peripheral steepened zone called ring zone, coinciding with the corneal clearance seen in the fluorescein pattern, under the edge of the optic zone and the reverse curve zone. It is clear that centration of the treatment depends of the lens location in the closed eye during the night. The dioptric change in apical corneal power that results from central corneal flattening in orthokeratology has been reported to correlate strongly with the change in refractive error. Potapova et al. published a study performed with CRT fitted in 29 healthy patients(9). They evaluated the topographic changes after 1 month of wearing CRT contact lenses. They found that mean corneal K-readings decreased at month of wearing, being statistically significant when was compared with baseline ($p<0.05$).

In another study performed by Lu et al. they evaluated the effect of one night CRT wearing for hyperopia in the topographic parameters(10). They found that the central cornea steepened, and the med-periphery flattened, returning to baseline at 28 hours of discontinuation.

Villa-Collar et al. investigate the short-term variations in corneal topography within the first 3 hours of CRT lens wear under open eye conditions and the recovery of the effect during an additional 3-hour period after lens removal(11). Overall, patients with -4.00 D showed that changes progressed more rapidly than in the patients with -2.00 D, and they also took more time to recover after lens removal. On another hand, Queiros et al. compared the topographic changes in the horizontal meridian between CRT contact lenses and LASIK refractive surgery(12). They found a statistically significant increase in the mean corneal K-readings more pronounced after CRT treatment than LASIK.

It was assumed that the cornea is molded towards the back surface shape of the contact lens as a result of the pressure exerted by the lens over the cornea. Initially, was generally supposed that the corneal tissue response to orthokeratology was an overall bending and consequent a flattening(13). There is some controversial regarding corneal back surface suffers changes by the orthokeratology wearing. Yoon et al. found that no statistically significant changes in posterior corneal apical radius of curvature during 14 days of overnight orthokeratology(14). However, Gonzalez-Mesa et al. found that a significant reduction in anterior chamber depth and flattened of posterior corneal radius was observed after 15 days of wear CRT contact lenses(15). More studies should be conducted to clarify what is the corneal response to orthokeratology pressure.

The corneal epithelium is the most altered tissue for orthokeratology lenses. Choo et al. performed a study in an animal model to evaluate the effect of CRT lenses over corneal epithelium and they found that epithelial thickness in myopic corrected eyes showed progressive thinning in the center and progressive thickening in the mid-periphery with increased lens wearing time(16). With humans, Wang et al. found that immediately after removal of the CRT lens, after one night of wearing, the central epithelium was 5.1±4.5% thinner than baseline and the epithelium in the mid-periphery showed significant thickening(17). Others authors found after one month of CRT wearing that the central epithelium thinned by 7.3%, and the mid-peripheral epithelium thickened by 13% being recovered the baseline values three days after the study completion(18-20). A short-term effect of overnight orthokeratology on corneal cell morphology has been studied with CRT lenses. Nieto-Bona et al. evaluated with a confocal microscope the effect of orthokeratology lens wearing over all layers of the cornea(21). They found that no significant changes in either endothelial cell, neither stromal cell density or nerve plexus were observed after 1 month of CRT wearing, suggesting that the corneal epithelium is the principal structure affected by the mechanical forces exerted by the orthokeratology lenses, in this case CRT. The same research group performed the same study but long-term, evaluating the corneal morphology after one year of CRT wearing finding that no significant changes in endothelial cell density were observed over time but polymegathism increased significantly and corneal thickness, Bowman layer thickness, sub-basal plexus thickness and epithelial thickness were reduced in the central cornea but the stroma was thickened(22). Apart of corneal epithelium, only it has been studied the endothelium in orthokeratology wearers and the results were similar to Nieto-Bona et al. study (23)

Orthokeratology lens reduces the corneal sensitivity that it recovers with cessation of lens wear. Changes to nerve morphology induced by OK lens wear, however, appear to recover more slowly (24). Biomechanical parameters have also been studied in orthokeratology. González- Méijome et al. studied the correlation between corneal response to corneal refractive therapy and the biomechanical properties of the cornea (25). They found a faster response and recovery for corneas with lower resistance. On the other hand, besides corneal epithelium permeability, Yeh et al. studied the corneal biomechanical properties after CRT lens wearing (26). Orthokeratology caused a decreasing corneal hysteresis and corneal resistance factor, but the changes were not clinically significant compared with diseased and postsurgical cases. Asian individuals with lower baseline corneal hysteresis responded slower to the therapy based on early uncorrected VA and over-refraction measurements.

There are several studies regarding visual outcomes with orthokeratology contact lenses. It is expected to get reductions of myopia up -4.00 D without complications. Koffler et al. found that they can correct myopia up -7.00 D with CTR lenses (27). Also, all patients improved their visual acuity without correction. They concluded that the CRT lens is an effective modality for temporary myopic correction for a restricted subset of myopic candidates. Those with a spherical manifest refraction between 1.00 and 6.00 D and up to 1.50 D of astigmatism can expect a good outcome with these lenses.

Changes in the astigmatism with different toric orthokeratology lens designs have been shown to be effective in reducing astigmatism greater than 1.50 D compared the safety and efficacy of toric versus spherical orthokeratology lenses in moderate and high astigmatism, demonstrating that the toric design helps to reduce lens decentration (28).

Visual outcomes have also been evaluated in children. Walline et al. designed a COOKI study to investigate the effects on visual quality and adverse events of orthokeratology fitted in children(29). The conclusion was Overnight corneal reshaping contact lenses are efficacious for young myopic patients, and no children experienced a serious adverse event during the study.

Advancement in lens material not only has increased the rate at which orthokeratology can reach its maximum effect, but also it has increased safety. The original lens material used in orthokeratology, polymethyl methacrylate, had a negligible oxygen transmission, causing them to be unsafe for extended wear. The material used in today's overnight extended wear gas permeable lenses have a Dk value ranging from 49 to 163, indicating high oxygen permeability and reduced risk of infection. There has been a total of 123 instances of microbial keratitis in orthokeratology patients reported between 1997 and 2007. Most of the reported cases were found in East Asian children ranging in age from 9 to 15 years of age, mainly due to inappropriate lens care, patient not following practitioner's instructions, and continuation of lens wear despite discomfort. Common organisms found were Pseudomonas aeruginosa and Acanthamoeba. Another studies found an incidence of microbial keratitis of 7.7 per 10,000 patient/year of wear, making orthokeratology wearers only slightly more susceptible to infection than daily soft contact lens wearers at 4.1 per 10,000 and better than 30-day extended wear silicone hydrogel lens wearers to be 14.4 per 10,000 patient/year of wear(2). Also, the incidence of orthokeratology is slightly less than LASIK surgery with an incidence of 9 per 10,000 patient/year(30). Arance-Gil et al. showed a case of microbial keratitis by Acanthamoeba in a CRT lens wearer after having bathed in a swimming pool that was poorly maintained(31). Another two cases of ulcers have been described in 2005 provoked by bacterial infection, probably due to wrong cleaning and maintenance of the lenses(32).

It is clear that cleaning and maintenance of orthokeratology lenses is critical for diminishing or avoiding future ocular infection. No studies have been performed to evaluate the best system to maintain the orthokeratology lenses. Only there is a study compared different solutions in CRT wearers and they concluded that patients preferred Boston Simplus to Boston Advance with corneal reshaping lens wear when evaluated for comfort, unaided daytime vision, and care and handling (33).

Corneal edema, inflammation, dry eye symptoms, corneal staining and corneal pigmentation has been considered as adverse events during orthokeratology contact lens wear. Haque et al. performed a study to assess the corneal swelling response to two myopic correction corneal refractive therapy (CRT) lenses of varying Dk/t values, worn for a single night(19). They found that the higher-Dk/t material caused significantly less overnight corneal and stromal swelling than the lower-Dk/t material, which reinforces the need to prescribe lenses with high Dk/t for overnight wear. Neither central epithelial thinning nor paracentral thickening are significantly affected by Dk/t. Similar corneal swelling has been reported with other orthokeratology designs.

The presence of a pigmented ring in the cornea of orthokeratology wearers has attracted interest from the clinical community because this has been reported in a significant number of Asian patients from Hong Kong and Taiwan(34, 35). Rah et al. reported various cases in CRT wearers being more prominent in patients with dark iris and in patients with higher baseline refractive errors(36). They concluded that it does not appear to affect visual acuity nor does it appear to be adverse in nature. Also, Gonzalez-Meijome et al. reported two cases of pigmentation ring in Caucasian wearers, reducing the potential role of an ethnic link(37).

Regarding inflammation of the ocular surface Gonzalez-Perez et al. (38, 39) evaluated the concentration of different mediators of inflammation, related with dry eye after orthokeratology, soft contact lenses in continuous-wear basis and LASIK surgery. They found an increase of some pro-inflammatory molecules in orthokeratology wearers, related with the epithelial changes done by the reverse geometry lenses. Carracedo et al. evaluated the signs and symptoms of dry eye in CRT wearers and they did not find that orthokeratology produced symptoms or signs of ocular dryness, which could be a potential advantage over soft contact lenses in terms of contact lens-induced dryness. This increasing of inflammatory mediators in tears of orthokeratology wearers is not clinically relevant. On another hand, the corneal staining seems similar with gas permeable lens in daily wear basis and overnight orthokeratology(40). A short-term study of the same researchers shown improves in goblet cells density and dry eye symptomatology in orthokeratology wearers (41).

Finally, the severity of corneal changes and adverse events reported above should be evaluated in terms of reversible capability of the therapy. It is evident that the severity would be greater if corneal changes by orthokeratology are irreversible. The most important studies about that have been performed with CRT lenses (22), demonstrating that the majority of corneal changes provoked by orthokeratology lenses are reversible after contact lens discontinuation(42).

CASE 1

Diagnosis and treatment

A 14-year-old woman with myopia since age 11, living in Madrid, Spain. She has never worn contact lenses. She refers poor far distance vision with frequent changes in prescription. During her last check-up, orthokeratology treatment was recommended to control the myopia. Her mother had myopia and her father was emmetropic. There is no other relevant systemic or ocular history.

Current refraction: OD -2.00 D VA 0.0 logMAR y OI -1.75 D VA 0.0 logMAR. Topography: OD: 43.00 D x 43.50 D; e (0.42); OS: 42.80 D x 43.80 D e (0.46). Myopia control treatment began with orthokeratology. The parameters of fitted lenses were (image 1): OD CRT standard 85-525-32-10.50 and OS CRT DA 83-525/550-32-10.50. A periodic checks-up were made during 12 months with axial length measurement.

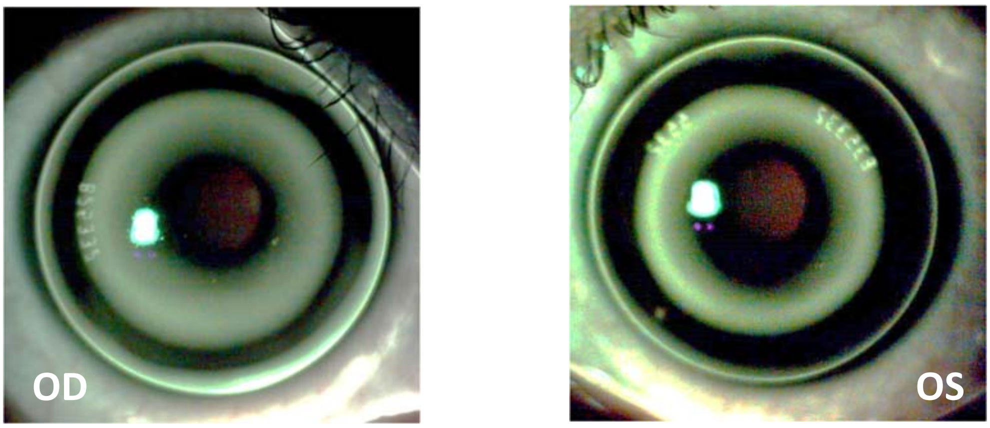


Image 1. Fitted lenses

Results

The evolution of high contrast VA and axial length variation are shown in Table 1. The comparison of the initial topography and after 12 months is shown in image 2. After 12 months, the reversibility of the treatment was assessed after 1 month without orthokeratology lenses. The axial length values did not change. Subjective refraction after a month without wearing the lenses was similar than baseline.

	Without refraction		With refraction		Axial Length (mm)	
	VA OD	**VA OS**	**VA OD**	**VA OS**	**OD**	**OS**
BASELINE	0.68	0.68	0.00	0.00	25.00	24.73
1N	0.30	-0.2	-0.1	-0.2	--	--
1W	-0.1	-0.1	-0.1	-0.1	--	--
1M	-0.1	-0.2	-0.1	-0.2	25.00	24.78
3M	-0.16	-0.18	-0.16	-0.18	24.96	24.78
6M	-0.2	-0.1	-0.2	-0.1	24.89	24.72
12M	-0.14	-0.2	-0.14	-0.2	24.94	24.78
POST-TREATMENT	0.66	0.44	-0.14	-0.14	25.02	24.86

Table 1. Visual Acuity and Axial Length values

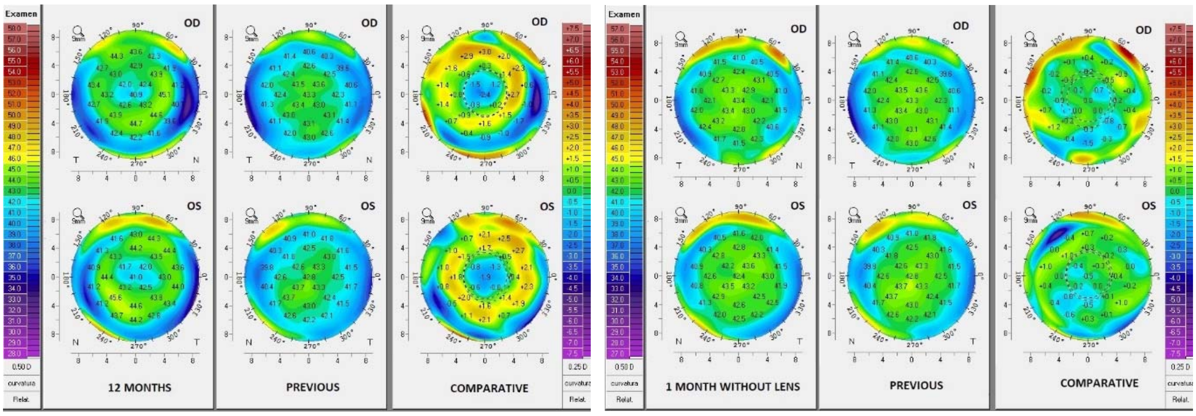


Image 2: Comparative topographies during the treatment and after treatment

<u>Conclusions</u>

It has been observed how the visual acuity and refraction kept stable during all time of wearing, as well as the axial length, which indicates a stabilization of a possible myopic progression. Currently, orthokeratology is proposed as an effective and safe myopic control treatment compared to other pharmacological or optical correction alternatives.

CASE 2

Diagnosis and treatment

A 15-year-old woman who wears soft contact lenses (CL). She came to the clinic because of her myopia since she was 10 years old and her family has myopia.

Current refraction: OD -3.00 D, OS -3.25 D ; VA RE: 0.08 LE:0.04 (LogMAR); Topography: OD: 43.8D x 44.1D e(0.67); OS: 43.7D x 44.6D e(0.72).

Image 1 shows a centered and optimal fluorogram during the fitting. OD CRT 8.5-550-32 -10.50 and OS CRT DA 8.5-550&575-31-10.50.

After fitting, the insertion and removal of the lens using an artificial tear (AT) is explained, as well as the importance of good hygiene with the maintenance system.

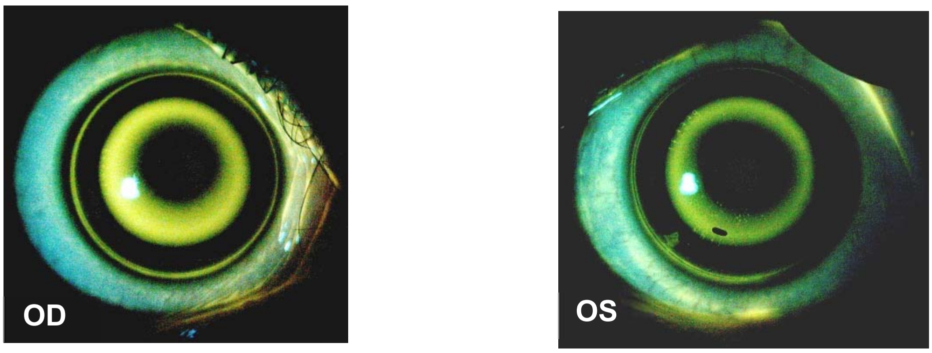


Image 1: Orthokeratology contact lenses fluorogram

Results

After 3 months, a central island pattern was observed in the topography (Image 2). This caused a decrease in VA, being more marked at 3 months (Table 1). Furthermore, the Efron scores showed a central staining of grade 2 (Image 3). The fitting of the lenses was revised to know the origin of the central island, and it was observed a good fluorogram. The manipulation was checked, observing that the patient did not insert the lenses with tears; the procedure of manipulation and cleaning of the lenses was repeated to avoid possible complications.

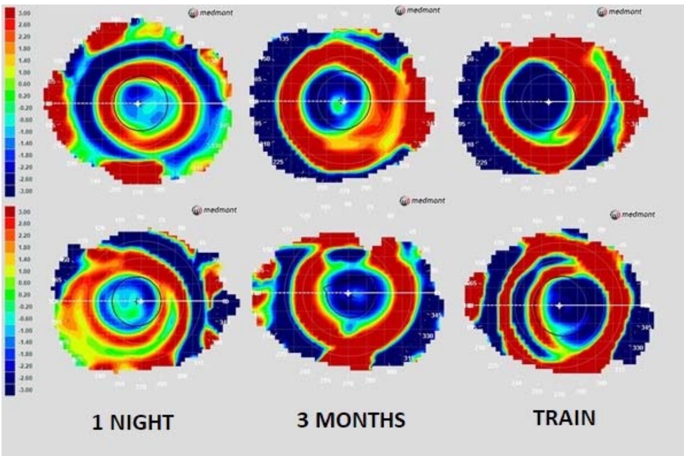
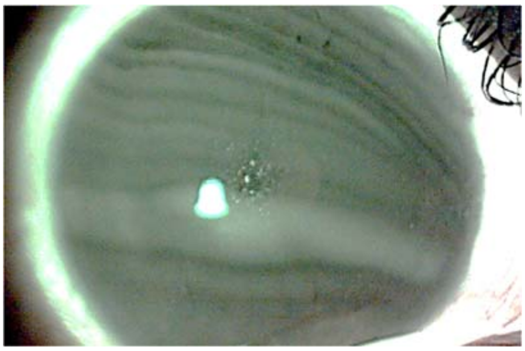


Image 2: Topographies obtained during the treatment. Upper (OD). Lower (OS)

Table 1: Visual acuity logMAR

	Without refraction		With refraction	
	VA OD	VA OS	VA OD	VA OS
BASELINE	0.9	0.9	0.08	0.04
1N	0.3	0.1	0.00	0.00
1W	0.00	0.00	0.00	0.00
1M	0.1	0.04	0.1	0.04
3M	0.1	0.2	0.1	0.2
6M	0.00	0.08	0.00	0.08
12M	0.3	0.7	0.1	0.1

Image 3: Central corneal staining



Conclusions

When a central island is observed, it may be due to an excessive central sagitta or it may be caused by a central corneal staining by adherence of the lens, so we must know what the origin is. For the insertion and removal of the OK contact lens, it is important to use artificial tears to reduce corneal staining and future complications associated with it. Therefore, if the central island persists due to not comply with guidelines, the practitioner should discontinue the treatment to avoid further complications.

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