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ORIGINAL ARTICLE

Corneal higher-order aberrations in amblyopia

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PURPOSE. *To investigate the amount, type, and role of corneal higher order aberrations in both isotropic and anisometropic amblyopic adult patients.*
METHODS. *A total of 125 eyes of 78 patients with age ranging from 18 to 67 years (30 patients with unilateral amblyopia, 17 with bilateral amblyopia, and 31 normal eyes considered as the control group) were included. All eyes received a comprehensive ophthalmologic examination that included corneal topographic and aberrometric analysis with the CSO system. The aberrometric study was performed for a 6-mm pupil using different root mean square (RMS) parameters. Additionally, the ocular residual astigmatism (ORA) was also calculated and analyzed. A comparative analysis of the refractive and aberrometric data between groups was performed.*
RESULTS. *In the unilateral amblyopia group, statistically significant differences between the amblyopic and non-amblyopic eye were found in cylinder ($p=0.003$), best-corrected visual acuity (BCVA) ($p<0.001$), total RMS ($p=0.015$), and astigmatic RMS ($p=0.019$). Statistically significant differences between the bilateral amblyopia and control groups were observed in sphere ($p=0.025$), cylinder ($p=0.005$), and BCVA ($p<0.001$). When comparing isometropic and anisometropic bilateral amblyopic eyes, significant differences in total ($p=0.025$) and astigmatic RMS ($p=0.013$) were detected. Higher but nonsignificant amounts of primary coma were found in isometropic eyes (0.25 µm anisometropic vs 0.43 µm isometropic, $p=0.09$). Regarding the ORA, no significant differences between groups were found ($p\geq0.224$).*
CONCLUSIONS. *In unilateral and bilateral amblyopia, lower order aberrations are the main refractive factors leading to amblyopia. Higher order aberrations could have a bilateral amblyogenic effect in those cases where isometropia is present. (Eur J Ophthalmol 2010; 20: 12-20)*

KEY WORDS. *Amblyopia, Anisometropic amblyopia, Corneal higher order aberrations, Corneal topography, Isometropic amblyopia*

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INTRODUCTION

Amblyopia is an abnormally low visual acuity due to a disturbing foveal stimulation at early age. There are 3 major causes of amblyopia according to the classification of Von Noorden and Campos (1): strabismus, refractive, and deprivation. Strabismus can lead the nondominant eye to amblyopia due to cerebral suppression to avoid double vision. Vision deprivation caused by complete ptosis, media opacities, occlusion, or atropinization is another cause of amblyopia (amblyopia ex anopsia). There can also be a refractive cause for amblyopia which includes anisometropia, ametropia, and meridional astigmatism. Hyperopia has a greater potential to induce anisometropic (2, 3) as well as isometropic (4) amblyopia. Anisometropia between 1 and 4 years of age is an important factor leading to amblyopia (5). Also the presence of constant or increasing astigmatism (5), astigmatism of more than 1.50 diopters (6), or oblique astigmatism (7) increases the risk of developing amblyopia.

Amblyopia can usually be explained by one or more of these causes. However, enigmatic cases defined as idiopathic amblyopia can be found (8). In 2007, Agarwal et al (9) defined aberropia as a probably refractive entity which can lead to a masked amblyopia. Aberropia is defined as a refractive error which cannot be corrected by spherocylindrical lens combination and it is referred to as higher order aberrations (HOAs), i.e., coma, or spherical aberration. Prakash et al (10) described a case of idiopathic unilateral amblyopia possibly due to the asymmetry in the pattern of HOAs between both eyes. The authors suggested that wavefront evaluation has given insight into the etiology of unexplainable amblyopia. On the other hand, Kirwan and O'Keefe (11) emphasized that HOAs did not play a role in the development of amblyopia in these patients in whom the cause of amblyopia is known.

The first corneal surface is the most important source of optical errors. The interface air-cornea is the main contributor to the total eye power due to the large difference in refractive indexes between air and cornea (12). Anterior corneal wavefront aberrations depend on many factors, increasing in magnitude with age according to several authors (13, 14). However, Fujikado et al (15) stated that corneal aberrations are not significantly correlated with age. On the other hand, it has been proved that myopic children present greater levels of HOAs (16). These corneal HOAs can have an important impact on ocular aberrations and then on final visual quality. Brunette et al (17) concluded that ocular aberrations decreased progressively throughout childhood, adolescence, and early adulthood, reaching a minimum level during the fourth decade of life and increasing after progressively with age.

Amblyopia is developed during the first years of life and normally visual acuity becomes stable at the age of 8 to10 years (18). If the level of corneal aberrations is high during childhood, it could affect visual acuity development. In these cases, if amblyopia is present and no other causes of amblyopia can be found, HOAs could be considered as responsible for amblyopia development. In other words, HOAs could be considered as another refractive cause of amblyopia. It is supposed that the tendency to higher HOA levels in these cases will be maintained throughout life in comparison with people with normal levels from the beginning of life. The aim of the present study was to investigate the amount and type of HOAs in both isotropic and anisometropic amblyopic adult patients. To our knowledge, this is the first study that shows the distribution of corneal HOAs in a significant sample of amblyopic eyes.

MATERIALS AND METHODS

This study is a retrospective analysis of corneal aberration data of patients screened for refractive surgery from April 2006 to April 2007 at Vissum Instituto Oftalmológico de Alicante. A total of 125 consecutive eyes of 78 patients (30 patients with unilateral amblyopia, 17 with bilateral amblyopia, and 31 normal eyes considered as the control group) were included. Amblyopia was defined as a best-corrected visual acuity (BCVA) of 0.8 (20/25) or less in one or both eyes without any organic reason. In all unilateral amblyopic cases, the contralateral eye was included and considered as a control for comparison with the amblyopic eyes. In addition, the first 31 consecutive cases without amblyopia were included and considered as the control group for comparing with cases of bilateral amblyopia (Fig. 1). Exclusion criteria were strabismus, ectatic corneal disease (no paracentral corneal steepening and no slit-lamp signs of ectasia as stromal thinning, Fleischer ring, or Vogt striae) and any growth anomaly in the eye anterior segment and fundus such as corneal scar, retinopathy, or optic nerve disease that could explain low vision.

Patient age ranged from 18 to 67 years (mean 38.44 ± 10.21 years). A total of 35 women (44.87%) and 43 men (55.13%) were included. Amblyopia cases were divided into 2 groups according to the following criteria: cases with unilateral amblyopia were designated as group 1 and cases with bilateral amblyopia were designated as group 2. In each group, series with isometropia and anisometropia were also created. Anisometropia was defined as a difference in sphere of 3 diopters (D) or more and/or difference in astigmatism of 2 D or more. In group 1, 19 eyes with anisometropia, 11 with isometropia, and 30 non-amblyopic eyes were included. In group 2, 12 eyes were anisometropic and 22 isometropic (Fig. 1). In addition, a control group of 31 normal eyes was established for comparison with bilateral amblyopic eyes (Fig. 1).

Each patient underwent a comprehensive ophthalmologic examination that included uncorrected visual acuity (UCVA), best-corrected visual acuity (BCVA), subjective refraction (manifest and cycloplegic), papillary examination, ocular motility, stereopsis (TNO test), applanation tonometry, slit-lamp biomicroscopy, dilated fundus examination, ultrasonic pachymetry (DGH500 US pachymeter; DGH Technology Inc., Exton, PA, USA), and corneal topography (CSO; Firenze, Italy).

Corneal aberrations were derived from the corneal topography data obtained with the CSO system. The software of

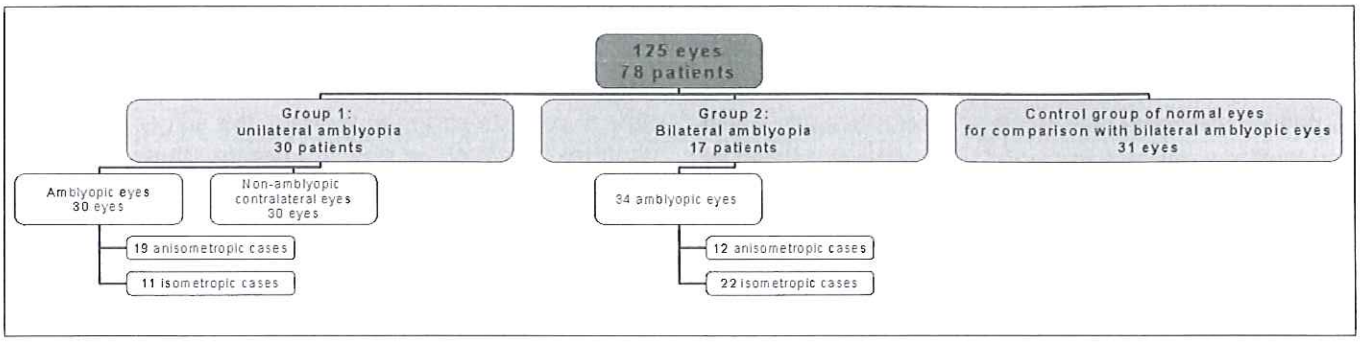

Fig. 1 - *Distribution of normal and amblyopic cases in the sample of eyes that was analyzed.*

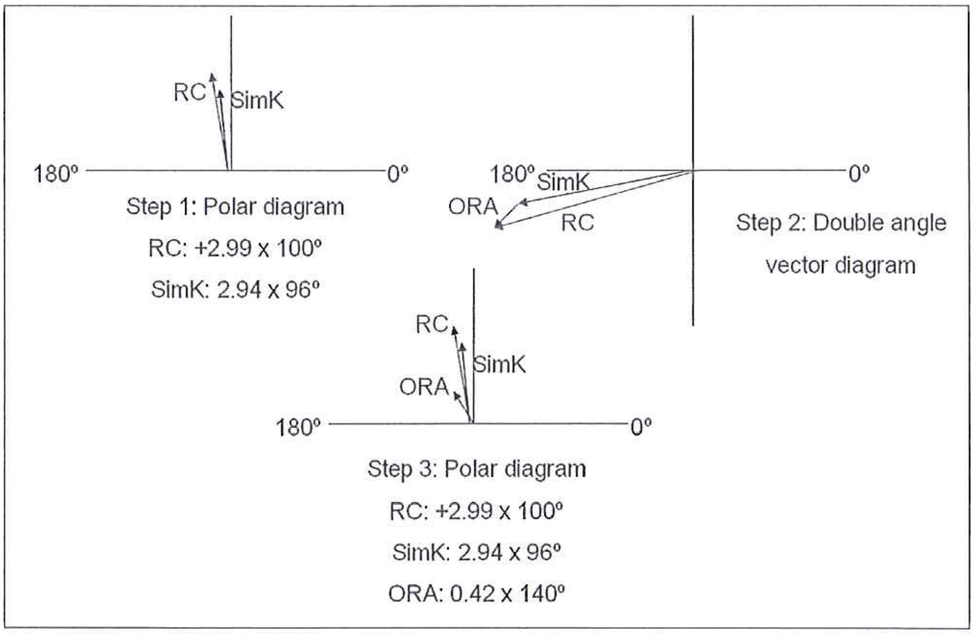

Fig. 2 - *Calculation of ocular residual astigmatism (ORA). Step 1* (upper left)*: polar diagram of refractive cylinder at the positive axis (calculated to the corneal plane) and corneal astigmatism from simulated keratometry. Step 2* (upper right)*: the double angle vector diagram showing a "doubling" of the angles without a change in the astigmatic magnitudes. Step 3* (lower)*: polar diagram displaying the ORA as it would appear on the eye. SimK = astigmatism from simulated keratometry obtained with the corneal topographer; DC = refractive or manifest astigmatism.*

this topography system, the EyeTop2005 (CSO), performs the conversion of the corneal elevation profile into corneal wavefront data using Zernike polynomials with an expansion up to the seventh order. In all cases, the aberrometric study was performed for a 6-mm pupil. The following root mean square (RMS) parameters were calculated: total, coma-like (computed for the third, fifth, and seventh order Zernike terms), spherical-like (computed for the fourth and sixth order Zernike terms), primary coma (computed for the Zernike terms $Z_3^{\pm 1}$), and higher order residual aberrations (computed with all Zernike terms except for those corresponding to the primary coma and spherical aberration). Additionally, the Zernike term corresponding to the primary spherical aberration was also reported with its sign (Z_4^0). The pupil center was used as a reference for centration of the aberrometric analysis.

In order to check the relevance of corneal astigmatism in amblyopic and normal eyes, the ocular residual astigmatism (ORA) was also calculated. This parameter is quantified by calculating the vectorial difference between refractive (calculated to the corneal plane) and corneal astigmatism (19, 20). The ORA is also known as intraocular (21), lenticular (22), and noncorneal astigmatism (23). The following steps were performed in each analyzed case for calculating the ORA (Fig. 2):

1) Representation of refractive and topographic cylinder vectors in a polar diagram: refractive cylinder at the positive axis (calculated to the corneal plane) and corneal astigmatism of simulated keratometry.
2) The double-angle vector diagram: it shows a "doubling" of the angles without a change in the astigmatic magnitudes.

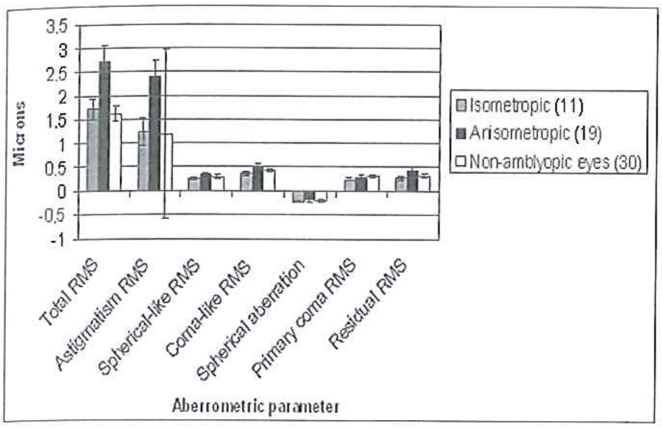

Fig. 3 - *Aberrometric outcomes for group 1 divided into anisometropic* (black bars), *isometropic* (grey bars), *and non-amblyopic* (white bars) *subgroups. RMS = root mean square. Primary coma: terms $Z_3^{\pm 1}$. Primary spherical aberration: term Z_4^0. Spherical-like: terms corresponding with fourth and sixth order. Coma-like: terms corresponding with third, fifth, seventh order. Residual aberrations: higher order without considering the terms Z_4^0 (primary spherical aberration) and $Z_3^{\pm 1}$ (primary coma).*

3) Calculation of the vectorial difference in the polar diagram, showing the ORA as it would appear on the eye.

Statistical analysis was performed with the SPSS statistical software package version 10.1 for Windows (SPSS, Chicago, IL). Normality of the analyzed data was investigated by means of the Kolmogorov-Smirnov test. With this test it was proved that the use of parametric statistics was not appropriate for our sample data. Therefore, the Mann-Whitney *U* test for unpaired samples was used for comparing the clinical data of amblyopic and non-amblyopic eyes, using a level of significance of $p<0.05$ in all cases. The following parameters were compared and analyzed in groups 1 and 2 and considered as main outcomes measures: manifest sphere and cylinder (DC), ocular residual astigmatism, BCVA, keratometry, corneal asphericity, and RMS for different types of corneal aberrations (total, astigmatism, primary coma, primary spherical aberration, residual, coma-like, and spherical-like).

In addition, the Kruskal-Wallis test was performed for comparing isometropic, anisometropic, and normal eyes in each group (1 and 2) using in all cases the same level of significance ($p<0.05$). For the post hoc multiple comparisons, the Mann-Whitney test was used with Bonferroni adjustment in order to avoid the experimental error rate.

RESULTS

Unilateral amblyopia group (group 1)

Table I summarizes refractive and corneal asphericity results in group 1. The mean DC was −2.47 D for amblyopic eyes and −1.20 D for normal eyes. Mean BCVA was 0.64 and 0.99, respectively. Statistically significant differences in DC and BCVA were observed in this group. Differences between amblyopic and normal eyes in sphere were not statistically significant (mean values, −2.4 D and −1.28 D, respectively) (Tab. I). In addition, no statistically significant differences were found in ORA between amblyopic and non-amblyopic eyes ($p=0.723$).

Table II summarizes corneal aberrometry outcomes obtained in group 1. Statistically significant differences in total ($p=0.015$) and astigmatic RMS ($p=0.019$) were observed in this group between amblyopic and non-amblyopic eyes. Mean total RMS was 2.34 μm and 1.63 μm in amblyopic and non-amblyopic eyes, respectively. Mean astigmatic RMS was 1.96 and 1.19 μm, respectively. No statistically significant differences were found in the rest of the aberrometric parameters (Tab. II).

Figure 3 shows the aberrometric data in group 1 for anisometropic, isometropic, and non-amblyopic eyes. Statistically significant differences ($p=0.047$) were found in the astigmatic RMS among these 3 subgroups. In addition, no statistically significant differences were found in sphere, ORA, and spherical equivalent among anisometropic, isometropic, and non-amblyopic eyes ($p\geq 0.137$).

Bilateral amblyopia group

Table III summarizes refractive and corneal asphericity results obtained in group 2. Bilateral amblyopic eyes were compared with a control group including normal subjects. Statistically significant differences in sphere ($p=0.025$), DC ($p=0.005$), and BCVA ($p<0.001$) were found. Mean sphere was −5.80 D in amblyopic eyes and −0.85 D in normal eyes. Mean cylinder was −2.25 D and −1.21 D and mean BCVA was 0.74 and 0.99 for amblyopic and normal eyes, respectively. A higher mean value of ORA was found for amblyopic eyes when compared to normal eyes, but differences did not reach statistical significance ($p=0.224$).

Table IV summarizes the corneal aberrometric results obtained in control and group 2. No statistically significant differences were found in any RMS value between amblyopic and control eyes.

Figure 4 shows the aberrometric outcomes in bilateral amblyopia (group 2) for anisometropic, isometropic, and control eyes. Statistically significant differences in total (p=0.025) and astigmatic RMS (p=0.013) were observed between isometropic and anisometropic eyes. Mean total RMS was 2.46 µm for patients with isometropia and 1.61 µm for patients with anisometropia. The astigmatic RMS was 1.94 and 0.97 µm, respectively. Higher although not statistically significant amounts of primary coma were found in isometropic eyes (0.25 µm anisometropic vs 0.43 µm isometropic, p=0.09). In addition, no statistically significant differences were found in the ORA among anisometropic, isometropic, and normal eyes (p=0.219).

DISCUSSION

The impact of HOAs on emmetropization and visual development is not fully understood. HOAs have been considered as responsible for the degradation in retinal image quality (24) and the subjective visual disturbances not solved by spectacle correction (25). In recent years, Agarwal et al (9) and Prakash et al (10) presented case reports of amblyopia whose development could be in relation to a refractive aberropic error. These studies suggested a possible amblyogenic effect of ocular aberrations different from sphere and cylinder in amblyopic eyes with significant amounts of HOA and no other factor leading to amblyopia. Indeed, it has been suggested that this aberropic error

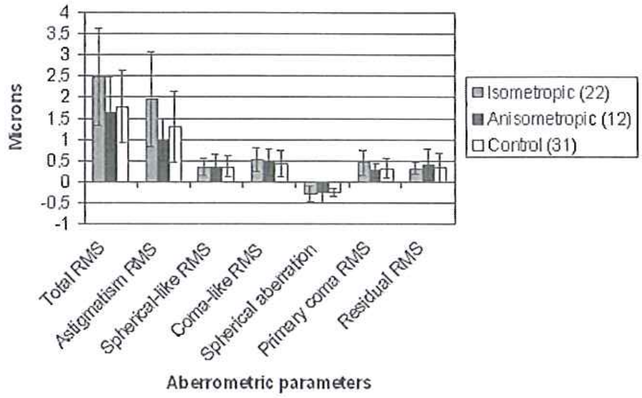

Fig. 4 - *Aberrometric outcomes for group 2 divided into anisometropic* (black bars)*, isometropic* (grey bars)*, and control* (white bars) *subgroups. RMS = root mean square. Primary coma: terms Z3±1. Primary spherical aberration: term Z40. Spherical-like: terms corresponding with fourth and sixth order. Coma-like: terms corresponding with third, fifth, seventh order. Residual aberrations: higher order without considering the terms Z40 (primary spherical aberration) and Z3±1 (primary coma).*

TABLE I - REFRACTIVE AND CORNEAL ASPHERICITY RESULTS FOR PATIENTS WITH UNILATERAL AMBLYOPIA (GROUP 1)

	Amblyopia eye,30 eyes	Non-amblyopic eye,30 eyes	P
Sphere (D)	−2.4±5.7 (−14.0 to 7.50)	−1.28±3.85 (−8.75 to 7.50)	0.314
Manifest refractive cylinder (D)	−2.47±1.95 (−8.00 to 0.00)	−1.20±1.08 (−4.00 to 0.00)	0.003*
Spherical equivalent (D)	−3.64±5.64 (−14.63 to 6.88)	−1.88±4.09 (−9.63 to 7.25)	0.122
BCVA	0.64±0.18 (0.15 to 0.88)	0.99±0.03 (0.90 to 1.00)	0.000*
ORA (D)	0.67±0.33 (0.00 to 1.57)	0.76±0.53 (0.00 to 2.06)	0.723
ASPH 45	−0.16±0.27 (−1.19 to 0.28)	−0.13±0.20 (−0.58 to 0.34)	0.554
ASPH 8	−0.26±0.24 (−0.83 to 0.53)	−0.31±0.21 (−0.74 to 0.11)	0.387
KM	43.96±1.23 (41.94 to 46.57)	43.92±1.25 (41.60 to 46.61)	0.941
Corneal astigmatism	2.00±1.51 (0.00 to 6.40)	1.17±1.01 (0.00 to 2.96)	0.015*

*Statistically significant differences.
BCVA = best-corrected visual acuity; ORA = ocular residual astigmatism; ASPH 45 = corneal asphericity for a 4.5-mm diameter area; ASPH 8 = corneal asphericity for an 8.0-mm diameter area; KM = mean keratometry in the 3-mm central area.

TABLE II - CORNEAL ABERROMETRY RESULTS FOR PATIENTS WITH UNILATERAL AMBLYOPIA (GROUP 1)

	Amblyopia, 30 eyes	Non-amblyopic eye, 30 eyes	p
Total RMS (μm)	2.34±1.37 (0.70 to 6.92)	1.63±0.84 (0.60 to 3.24)	0.015*
Astigmatic RMS (μm)	1.96±1.49 (0.09 to 6.63)	1.19±0.97 (0.14 to 3.01)	0.019*
Spherical-like RMS (μm)	0.31±0.13 (0.14 to 0.71)	0.30±0.14 (0.10 to 0.93)	0.888
Coma-like RMS (μm)	0.45±0.31 (0.21 to 1.45)	0.43±0.16 (0.16 to 0.88)	0.208
Primary spherical aberration (μm)	−0.19±0.13 (−0.38 to 0.25)	−0.20±0.10 (−0.42 to 0.10)	0.917
Primary coma RMS (μm)	0.28±0.16 (0.08 to 0.67)	0.32±0.11 (0.14 to 0.56)	0.083
Residual aberrations RMS (μm)	0.38±0.33 (0.12 to 1.50)	0.33±0.21 (0.10 to 1.20)	0.739

*Statistically significant differences.
Primary coma: terms $Z_3^{\pm1}$. Primary spherical aberration: term Z_4^0. Spherical-like: terms corresponding with fourth and sixth order. Coma-like: terms corresponding with third, fifth, seventh order. Residual aberrations: higher order without considering the terms Z_4^0 (primary spherical aberration) and $Z_3^{\pm1}$ (primary coma).
RMS = root mean square.

TABLE III - REFRACTIVE AND CORNEAL ASPHERICITY RESULTS FOR PATIENTS WITH BILATERAL AMBLYOPIA (GROUP 2) COMPARED TO THE OUTCOMES OBTAINED IN A CONTROL GROUP

	Amblyopia, 34 eyes	Normal eyes, 31 eyes	p
Sphere (D)	−5.80±5.51 (−15.00 to 5.00)	−0.85±3.22 (−5.75 to 5.00)	0.025*
Manifest refractive cylinder (D)	−2.25±1.68 (−5.50 to 0.00)	−1.21±0.96 (−3.50 to 0.00)	0.005*
Spherical equivalent (D)	−6.83±5.24 (−16.50 to 4.13)	−1.45±3.17 (−6.38 to 4.50)	0.005*
BCVA	0.74±0.09 (0.50 to 0.88)	0.99±0.01 (0.8 to 1.50)	<0.001*
ORA (D)	0.96±0.68 (0.23 to 2.98)	0.78±0.61 (0.13 to 2.88)	0.224
ASPH 45	−0.15±0.39 (−0.56 to 0.95)	−0.11±0.19 (−0.61 to 0.29)	0.911
ASPH 8	−0.16±0.38 (−0.63 to 0.86)	−0.20±0.23 (−0.76 to 0.50)	0.318
KM	42.72±1.73 (38.47 to 47.61)	43.43±1.98 (37.94 to 47.52)	0.901
Corneal astigmatism	1.68±1.11 (0.00 to 4.50)	1.52±0.99 (0.00 to 4.50)	0.286

*Statistically significant differences.
BCVA = best-corrected visual acuity; ORA = ocular residual astigmatism; ASPH 45 = corneal asphericity for a 4.5-mm diameter area; ASPH 8 = corneal asphericity for an 8.0-mm diameter area; KM = mean keratometry in the 3-mm central area.

could be the explanation of some cases described as idiopathic amblyopia (26). This new concept of HOA as a factor leading to amblyopia has reinitiated interest in research in this area (26). In the present study, the prevalence and role of corneal HOAs in amblyopia have been analyzed. Specifically, in this retrospective study, global or ocular aberrometry has not been analyzed, because this kind of measurement was not a standard

TABLE IV - CORNEAL ABERROMETRY RESULTS FOR PATIENTS WITH BILATERAL AMBLYOPIA (GROUP 2) COMPARED TO THE OUTCOMES OBTAINED IN A CONTROL GROUP

	Amblyopia, 34 eyes	Normal eye, 31 eyes	p
Total RMS (µm)	2.16±1.11 (0.67 to 4.57)	1.76±0.84 (0.64 to 3.59)	0.193
Astigmatic RMS (µm)	1.24±1.04 (0.22 to 4.36)	1.27±0.83 (0.13 to 3.38)	0.290
Spherical-like RMS (µm)	0.34±0.24 (0.14 to 1.13)	0.34±0.25 (0.12 to 1.45)	0.378
Coma-like RMS (µm)	0.39±0.29 (0.17 to 1.15)	0.42±0.32 (0.13 to 1.67)	0.351
Primary spherical aberration (µm)	−0.28±0.21 (−0.80 to −0.10)	−0.27±0.11 (−0.63 to −0.07)	0.091
Primary coma RMS (µm)	0.27±0.26 (0.07 to 1.00)	0.31±0.23 (0.11 to 1.09)	0.494
Residual aberrations RMS (µm)	0.33±0.24 (0.15 to 1.36)	0.33±0.34 (0.10 to 1.86)	0.581

*Statistically significant differences.
Primary coma: terms $Z_3^{\pm1}$. Primary spherical aberration: term Z_4^0. Spherical-like: terms corresponding with fourth and sixth order. Coma-like: terms corresponding with third, fifth, seventh order. Residual aberrations: higher order without considering the terms Z_4^0 (primary spherical aberration) and $Z_3^{\pm1}$ (primary coma). RMS = root mean square.

in the refractive surgery screening examination. This was a limitation of this retrospective study. However, it must be considered that the cornea is the most important contributor to the total refractive power of the eye and the main source of ocular aberrations (12, 27). In addition, we have analyzed the impact of internal astigmatism in amblyopic and normal eyes by calculating the ORA, which is defined as the vectorial difference between refractive and corneal astigmatism.

In the unilateral amblyopia group, statistically significant differences between amblyopic and non-amblyopic eyes were found in DC and in 2 aberrometric parameters, corneal total and astigmatic RMS. Therefore, statistically significant differences were found in both corneal and manifest astigmatism. These results agree with previous works that defined the astigmatism as a factor leading to amblyopia (1, 5-7). It seems that although total corneal RMS was higher in unilateral amblyopic eyes, this higher magnitude was due to the significant level of corneal astigmatism that was present. Regarding internal astigmatism, no significant differences were found in ORA between amblyopic and non-amblyopic eyes. Therefore, in unilateral amblyopia the corneal astigmatism seems to be a key factor in developing amblyopia. It should be remembered that although adult patients have been included in this study, corneal astigmatism in healthy corneas remains stable during adolescence and adulthood, with the only significant changes toward against-the-rule patterns in the elderly (28, 29).

Corneal HOAs did not differ significantly between amblyopic and non-amblyopic eyes in the unilateral amblyopia group. In addition, corneal total and astigmatic aberrations were significantly higher in anisometropic eyes compared to isometropic and non-amblyopic eyes. Furthermore, no significant differences were detected in ORA between these subgroups. These findings re-mark the importance of corneal astigmatism in the development of unilateral anisometropic amblyopia. Regarding isometropic cases, no differences were found in corneal aberrations when compared to normal eyes. In this group of patients, hyperopia has been previously stated to have a great potential in amblyopia development (30). In our group of isometropic patients, we found a greater percentage of patients with hyperopia higher than 4 D (36.36% isometropic vs 10.52% anisometropic) in comparison with the anisometropic group.

Patients with bilateral amblyopia presented statistically significant higher levels of manifest sphere and DC when compared to a control group of normal eyes. No significant differences were found either in corneal aberrometric parameter or in ORA when comparing bilateral amblyopic and normal eyes. In any case, a trend for higher ORA was observed on average in the group of bilateral amblyopic eyes, although it did not reach statistical significance. When the bilateral amblyopia group was divided into isometropia and anisometropia, 2 other different tendencies could be observed: a greater percentage of high myopia (higher than 8 D) in patients with anisometropia (75% anisometropia vs 9.09% isometropia) and a greater percentage of astigmatism higher than 2.5 D in isometropic patients (16.67% anisometropia vs 40.91% isometropia). No significant differences were found in the ORA between anisometropic and isometropic eyes. When analyzing corneal aberrometry results, only isometropic eyes presented statistically significant higher values of corneal total and astigmatic RMS. This group of patients (bilateral isometropic amblyopia) is very interesting because the factors leading to amblyopia sometimes are not known or understood in these cases. Besides corneal astigmatism, in this group of eyes mean higher amounts of primary coma were observed when compared to anisometropic amblyopic eyes and also with normal eyes (primary coma RMS 0.25 µm anisometropia vs 0.43 µm isometropia). However, this difference did not reach statistical significance, probably due to the small sample size achieved in this study (12 anisometropic and 22 isometropic eyes). Therefore, in patients with bilateral isometropia, an aberrometric explanation for amblyopia could be possible, although corneal astigmatism seems to be the most important amblyogenic factor.

Results obtained in this study bring new insights into the field of amblyopia regarding the role of HO corneal aberrations. To our knowledge, this is the first study attempting to analyze the corneal HOA profile in amblyopic eyes and attempting to define its role in amblyopia development. Kirwan and O'Keefe stated that HOAs did not play a role in the development of amblyopia in those patients in whom the cause of amblyopia is known (11). In this study, astigmatism has been found to be an important factor in unilateral and bilateral amblyopia. Corneal astigmatism is the main differential factor between normal and amblyopic eyes when considering unilateral anisometropic and bilateral isometropic cases. In addition, it seems that internal astigmatism could also be an important factor in the development of bilateral amblyopia. Furthermore, no significant differences in corneal HOAs have been found in this study between normal and amblyopic eyes. However, primary coma aberration could have an important role in developing isometropic bilateral amblyopia, besides corneal astigmatism. It should be remembered that primary coma is one of the most disturbing HOAs that can be found in the eye (31).

In conclusion, in unilateral and bilateral amblyopia, lower order aberrations, sphere and cylinder, are the main refractive factors leading to amblyopia. It seems that HOAs could have a bilateral amblyogenic effect in those cases where isometropia is present. In future studies, corneal and global aberrations should be evaluated in those specific cases with the diagnosis of idiopathic amblyopia in order to prove whether HOA can be the main factor leading to amblyopia in these cases and also to evaluate the benefit of correcting them with excimer laser surgery.

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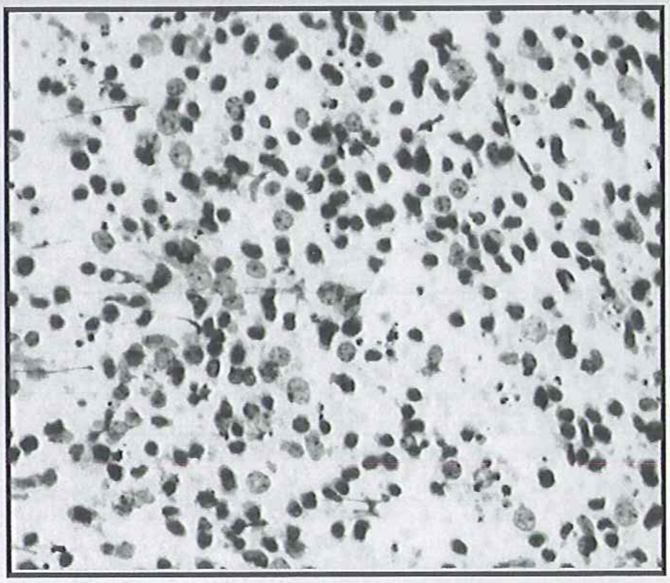

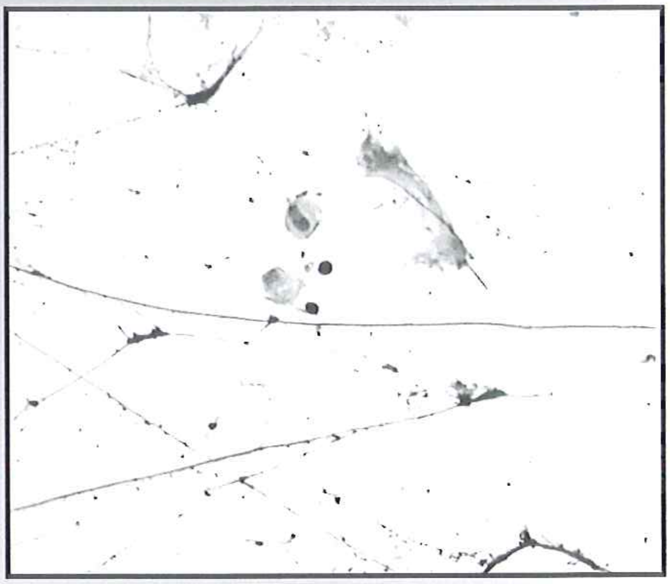

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