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Evaluation of choroidal thickness and retinal nerve fiber layer thickness in patients with unilateral amblyopia: a prospective study

Avaliação da espessura da coroide e da camada de fibras nervosas da retina em pacientes com ambliopia unilateral: um estudo prospectivo

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Abstract

Purpose: *to compare the Subfoveal choroidal thickness (SFCT) and Retinal Nerve Fiber Layer Thickness (RNFL) of amblyopic and normal fellow eyes. Design: Prospective, cross-sectional, observational case series. Methods: Forty patients age 12 to 41 years (mean 23.73 ± 6.42) with unilateral amblyopia were studied. Among them, 11(28.2%) patients had amblyopia secondary to strabismus and 29(71.8 %) had anisometropic amblyopia. Optical coherence tomography (OCT) of the peripapillary RNFL thickness of amblyopic and fellow eyes was performed. RNFL thickness measurements were taken from the superior, inferior, nasal and temporal quadrants in the peripapillary region. Also, subfoveal choroidal thickness (SFCT) was measured using spectral domain optical coherence tomography (SD-OCT).* ***Results:*** *Mean global RNFL thickness of the amblyopic and fellow eyes was 104.48 microns and 102.83 microns, respectively. The difference between the two groups was not statistically significant (p>0.05%). The thicknesses of the superior, inferior, nasal and temporal quadrants of the retinal nerve fiber layer between the amblyopic and normal fellow eyes showed no statistically significant difference (p>0.05%). However, the SFCT of amblyopic eye was 11 or more microns thicker than the fellow eye and this was statistically significant different (p<0.05%).* ***Conclusions:*** *This study demonstrated SFCT in amblyopic eyes was significantly thicker than the normal fellow eyes. The amblyopic process may involve the choroid, but not the prepapillary NFL.*

Keywords: *Amblyopia; Foveal thickness; Retinal nerve fiber layer thickness; Tomography, optical coherence; Optic nerve/pathology; Nerve fiber/pathology*

Resumo

Objetivo: comparar a espessura da coroide subfoveal (CSF) e da camada de fibra nervosa retinal (CFNR) de olhos amblíopes e normais. Design: série de casos prospectivos, transversais e observacionais. **Métodos:** Quarenta pacientes com idade entre 12 e 41 anos (média 23,73 ± 6,42) com ambliopia unilateral foram estudados. Entre eles, 11 (28,2%) pacientes apresentavam ambliopia secundária a estrabismo e 29 (71,8%) apresentavam ambliopia anisometrópica. Foi realizada tomografia de coerência óptica (TCO) da espessura da CFNR peripapilar do olho amblíope e do outro olho. As medidas de espessura da CFNR foram realizadas nos quadrantes superior, inferior, nasal e temporal na região peripapilar. Além disso, a espessura da coroide subfoveal (CSF) foi medida através de tomografia de coerência óptica de domínio espectral (TCO-DE). **Resultados:** A espessura média global da CFNR do olho amblíope e do outro olho foi de 104,48 mícrons e 102,83 mícrons, respectivamente. A diferença entre os dois grupos não foi estatisticamente significativa (p > 0,05%). As espessuras dos quadrantes superior, inferior, nasal e temporal da camada de fibras nervosas da retina entre o olho amblíope e o normal não apresentaram diferença estatisticamente significativa (p > 0,05%). No entanto, a CSF do olho amblíope foi 11 mícrons mais espessa (ou mais) do que a do outro olho – essa diferença foi estatisticamente significativa (p < 0,05%). **Conclusões**: Este estudo demonstrou que a CSF dos olhos amblíopes foi significativamente mais espessa do que a dos olhos normais. O processo amblíope pode envolver a coroide, mas ele não envolve a CFNR peripapilar.

Descritores: Ambliopia; Espessura da fóvea; Espessura da camada de fibras nervosas da retina; Tomografia de coerência óptica; Nervo óptico/patologia; Fibras nervosas/patologia

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Introduction

Amblyopia is a developmental disorder of vision in which there is reduced visual acuity in one or both eyes (most commonly unilateral) that is generally detected in 2-5% of the general population.[1] The pathogenesis of amblyopia includes the lack of adequate visual stimulation to the fovea secondary to strabismus, abnormal binocular interaction of visual information received by the two eyes, image blur from anisometropia and, less commonly, an obstruction along the visual axis.[2,3] Further, recent studies suggest that the amblyopic eye also may have retinal abnormalities, including changes in the retinal ganglion cells, the retinal nerve fiber layer (RNFL) and the optic nerve.[4,5] In Korea, Kang et al.[4] reported the alteration of the macula thickness in normal adults older than 20 years by performing Optical Coherence Tomography (OCT).

The choroid is an integral structure in the eye that accounts for most of the ocular blood flow which is of paramount importance to retinal and visual function. Moreover, thinning of the choroid may be involved in many retinal or optic nerve diseases. Some studies have found retinal abnormalities in amblyopic eyes. [5] These findings suggest that the choroid may be involved in amblyopia.

Optical coherence tomography (OCT) of the peripapillary optic nerve is a non-invasive test in which the thickness of the retinal nerve fiber layer (RNFL) is measured.

One study using optical coherence tomography (OCT) found that retinal or choroidal thickness (CT) in amblyopic eyes is thicker than in fellow and normal control eyes.[5] Another study found there was no significant difference in the macular inner retinal thickness in unilateral amblyopia patients.[6]

The purpose of this study was to compare changes in the subfoveal choroidal thickness and the retinal nerve fiber layer thicknesses of amblyopic and fellow eye subjects 12 to 41 years old using SD-OCT.

Methods

This study was performed from January 2018 to May 2018 on 40 patients who were diagnosed with unilateral amblyopia. Approval for this project was obtained from the institutional review board of Baqiyatallah University of Medical Sciences. The study was performed according to the tenets of the Declaration of Helsinki for research involving human subjects. Patients with unilateral amblyopia were consecutively enrolled and informed consent was obtained from all patients. The included subjects were patients whose difference in visual acuity was at least two lines between the normal and amblyopic eye on the Snellen visual acuity charts. Anisometropia was diagnosed in those patients whose spherical equivalence showed 2.0 diopters or greater difference between the two eyes. Clinical examinations included best corrected visual acuity, refraction error, slit lamp examination, extraocular movements, intraocular pressure and fundoscopy. Patients with a neurological disease or ocular diseases such as glaucoma or nystagmus, a history or evidence of intraocular surgery, history of cataract, retinal disorders or laser treatment, patients not cooperative enough for OCT examination and patients whose pupillary dilation was not sufficient were excluded from this study

All subjects were examined using an enhanced depth imaging (EDI) system (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany; wavelength: 870 nm; scan pattern: enhanced depth imaging), as reported previously.[6,7] All examinations were performed between 11 and 12 AM to avoid diurnal variation. The right eye was studied first, followed by the left eye. The center of each volumetric measurement was adjusted to the center of the fovea. We averaged the EDI image for 100 scans using the automatic averaging system. Choroidal thickness was measured from the outer portion of the hyper reflective line corresponding to the RPE to the inner surface of the sclera. The measurement of the retinal nerve fiber layer thicknesses started after dilatation of the pupils with tropicamide using SD-OCT system (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany; wavelength: 870 nm; scan pattern: enhanced depth imaging), as described elsewhere.[7-9] The location of the vitreoretinal interface and the retinal pigment epithelium defined the inner and outer boundaries and the distance between photoreceptor outer segments and retinal pigment epithelium was defined as the thickness of retina. All patients were measured three times and their average values were obtained.

Statistical Analysis

Descriptive statistics for continuous variables were calculated as means ± standard deviations. Spherical equivalent was defined as the spherical power plus half of the minus cylinder power. Snellen visual acuities were converted to logMAR VA for statistical analysis. Distributions of spherical equivalent, VA of the amblyopic eye, VA of the fellow eye and choroidal thickness were confirmed as normally distributed. The statistical analysis for the comparison of the retinal nerve fiber layer thicknesses between amblyopic and normal eyes in the patients with unilateral amblyopia was performed using a paired Student's t-test.P values less than 0.05 were considered to be statistically significant. The correlation between RNFL thickness and other continuous variables was determined using Spearman's rank correlation coefficient. All analyses were repeated for each quadrant (superior, nasal, inferior, temporal). Analyses were performed using statistical software (SPSS version 22.0; SPSS, Inc., Chicago, IL, USA).

Results

Forty patients with unilateral amblyopia were enrolled in this study. The mean age of the 40 patients included in the analysis was 23.73 ± 6.42 (12 to 40) years; 57.5% were female, and 42.5% were male. Additional baseline characteristics are listed in table 1. Amblyopia in 29 patients was due to anisometropia (asymmetric hyperopia) and in 11 patients was secondary to strabismus. The mean refractive error in eyes with anisometropic amblyopia was +4.25±1.25 diopter and was +1.00±0.75 diopter in the normal fellow eyes. The mean LogMAR best corrected visual acuity (BCVA) in eyes with anisometropic amblyopia and normal fellow

Table 1
Demographic and Clinical Description for Amblyopic Group and normal fellow Group

Amblyopic Group	Anisometropic Group	Strabismic Group
Number of cases	29	11
AGE (years)	25.12±5.73	22.34
SEX (male/female)	12/17	5/6
REFRACTION	+4.25±1.25	+1.50±0.50
VA(LOG MAR)	0.39±0.20	0.33±0.17

Table 2
Retinal nerve fiber layer thickness (µm) in normal and amblyopic patients (in all anisometropic and strabismic amblyopia cases)

	Amblyopic eyes	Normal fellow eyes	p-value
Mean nerve fiber layer thickness	104.48	102.83	>0.05
Nerve fiber layer superior	126.70	126.32	>0.05
Nerve fiber layer temporal	72.40	71.75	>0.05
Nerve fiber layer inferior	132.70	132.27	>0.05
Nerve fiber layer nasal	79.70	78.77	>0.05
Central macular thickness	264.00	255.13	>0.05
Central subfoveal choroidal thickness	356.53	345.15	<0.05

Table 3
Retinal nerve fiber layer thickness (µm) in normal and strabismic amblyopic patients

	Amblyopic patients	Normal	p-value
Mean nerve fiber layer thickness	98.45	99.55	>0.05
Nerve fiber layer superior	121.36	122.91	>0.05
Nerve fiber layer temporal	68.55	68.11	>0.05
Nerve fiber layer inferior	129.45	132.64	>0.05
Nerve fiber layer nasal	77.27	74.73	>0.05
Central macular thickness	242.64	243.19	>0.05
Central subfoveal choroidal thickness	374.36	352.73	<0.05

eyes were 0.39±0.20 and 0.00±0.00, respectively.

The mean refractive error in eyes with strabismus amblyopia and normal fellow eyes were +1.50±0.50 and +1.25±0.75, respectively and LogMAR BCVA were 0.33±0.17 and 0.00±0.00, respectively.

The mean total thickness and thicknesses of the four quadrants of the RNFL from the normal and the amblyopia are shown in table 2. There was no statistically significant difference found when comparing the thickness of the RNFL of the normal fellow eyes and that of the amblyopic eyes. Mean global RNFL thickness of the amblyopic and fellow eyes was 104.48 microns and 102.83 microns, respectively(p>0.05%).

The mean total RNFL thickness and also RNFL thickness of the 4 quadrants from eyes with anisometropic amblyopia had no significant difference with eyes with strabismic amblyopia (p>0.05). We compared the total RNFL thickness and RNFL thickness of 4 quadrants between eyes with anisometropic amblyopia and normal fellow eyes and also between eyes with strabismic amblyopia and their normal fellow eyes. There was no significant difference between them.

Central subfoveal choroidal thickness (CSCT) was significantly greater in amblyopic eyes (all eyes with anisometropic and strabismic eyes) than normal fellow eyes (p<0.001); however, there was no statistically significant difference between CSCT of eyes with anisometropic amblyopia and eyes with strabismic amblyopia (p>0.05). CSCT of eyes with anisometropic amblyopia was significantly thicker than patient,s fellow eye (p<0.001) , and also, CSCT of eyes with strabismic amblyopia was significantly thicker than normal fellow eyes (p<0.001) (Table 3 and Figure 1).

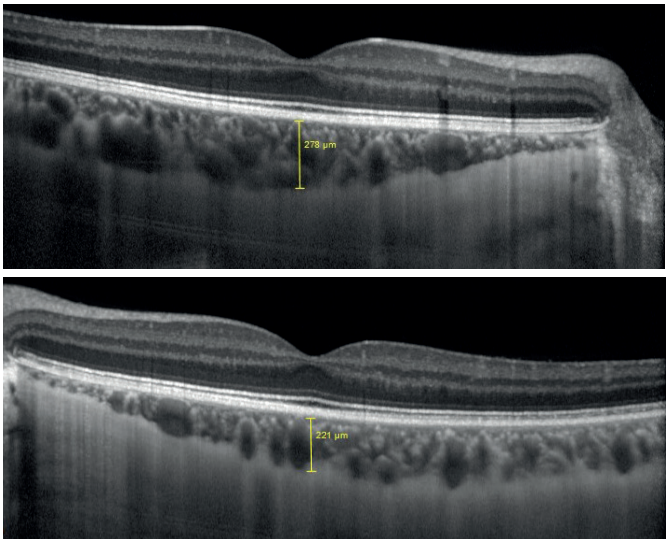

Figure1. Images from 1 measurement of choroidal thickness using swept-source optical coherence tomography of the amblyopic eye (top) and fellow healthy eye (bottom) of a patient with anisometropic amblyopia.

Discussion

It is unclear why there is a difference in RNFL thickness between amblyopia associated with strabismus versus refractive error. The findings suggest that different neural losses are associated with amblyopia of different etiologies.[5] The results in this

study revealed the subfoveal choroidal thickness in unilateral amblyopic eyes measured by SD-OCT was significantly thicker than that in the fellow eyes

In our study no meaningful difference was shown in global RNFL thickness or in the thickness in any of the four quadrants (superior, inferior, temporal, or nasal). Consequently, the results do not suggest that an optic neuropathy is a key aspect of anisometropic or strabismic amblyopia.

In a study by Baddini-Caramelli et al.[10] the thickness of the retinal nerve fiber layer of the amblyopic eyes and the normal eyes in the children with amblyopia was measured using scanning laser polarimetry. In these 21 patients whose mean age was 15 years (age range: 7-35 years), the total thickness of the amblyopic eyes and the normal eyes was 64.90±13.08 μm and 65.71±13.13 μm, respectively, and the thickness of the superior and the inferior quadrants of the amblyopic eyes and the normal eyes was 74.71±15.67 μm, 76.29±15.51 μm, 84.52±17.19 μm and 83.43±17.01 μm, respectively, showing no statistically significant difference.

Yen et al.[5] reported the thicknesses of the retinal nerve fiber layer of the amblyopic eyes and the normal fellow eyes in 18 patients with unilateral anisometropic amblyopia (mean age: 25.4 years) and 20 patients with strabismic amblyopia (mean age: 27.4 years), were 142.2±18.6 μm, 129.7±18.5 μm, 131.5±12.6 μm and 128.3±21.5 μm, respectively, with a statistical difference only in patients with unilateral anisometropic amblyopia. Moreover, the thickness of the retinal nerve fiber layer of the amblyopic eyes was thicker than that of the normal fellow eyes. However, the cause of this difference was not apparent; it may have been due to the retardation of the normal postnatal drop of ganglion cells.

In our study, in the comparison of the retinal nerve fiber layer thickness of the amblyopic eyes and the normal fellow eyes in 40 patients with amblyopia (mean age: 23.73 ± 6.42 years), the difference was not statistically significant between the amblyopic eyes and the normal fellow eyes. The results are in agreement with those reported by Baddini-Caramelli et al.[10] but are different from the results reported by Yen et al.[5]

In another study by Araki et al.[6] in 13 eyes of patients with unilateral amblyopia, they found an average subfoveal choroidal thickness of 353.7 ± 86.6 microns and the global

fellow eye SFCT was 281.1 ± 56.2 microns. Similarly, we found average subfoveal choroidal thickness and the global fellow eye SFCT 356.53 microns and 345.15 microns respectively, supporting our use of the fellow eye subfoveal choroidal thickness as an appropriate comparison group.

There are several limitations to our study, the most important being the fact that since patients enrolled in the present study had amblyopia due to anisometropia or strabismus, the results cannot be generalized to deprivational amblyopia. Another limitation of this study is that the number of patients with strabismic amblyopia was slightly small. Additionally, adjustment for the possible effects of age, sex, refractive errors, and axial length on RNFL thickness was not performed. In summary, our findings indicate that subfoveal choroidal thickness in amblyopic eyes is thicker compared with their fellow eyes. However; histological studies are needed to see whether the difference of the thickness has a clinical significance.

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