

Comparison of Macular and Retinal Nerve Fiber Layer Thickness in Amblyopic and Fellow Eyes

Ambliyopik ve Sağlam Gözlerde Maküler ve Retinal Sinir Lifi Tabakası Kalınlığının Karşılaştırılması

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ABSTRACT

Objective: The purpose of this study is to investigate the relationship between macular and peripapillary retinal nerve fiber layer thickness and amblyopia.

Methods: A total of 56 pediatric patients with hyperopic anisometropic amblyopia were evaluated in this study. As the control group, we used the patients' fellow eyes. A comprehensive eye examination was performed, including best-corrected visual acuity with Snellen charts (converted to logMAR for analysis), slit-lamp examination, fundus examination, cover and, cover-uncover testing, and ocular motility testing. The macular thickness, retinal nerve fiber layer thickness, axial length and optic disc area of both eyes were measured.

Results: The mean age was 7.25±1.89 years. For the amblyopic and fellow eyes, the mean best-corrected visual acuity was 0.33±0.20 logMAR and 0.0± 0.0 logMAR, respectively. Macular center thicknesses were 225,55±18,86 µm and 215,7±12,96 µm in amblyopic and fellow eyes, respectively. Macular 6mm ring thicknesses were 281,32±33,51 µm and 256,07±28,91 µm in amblyopic and fellow eyes, respectively. RNFLT were 108,39±11,59 µm and 104,61±8,43 µm in amblyopic and fellow eyes, respectively There was a statistically significant difference in the macular center thickness, in macular 6-mm ring area thickness and in RNFLT (p<0.05). There was a positive correlation between visual acuity of amblyopic eyes and macular thickness and RNFLT.

Conclusions: This study explored objectively measured retinal changes in amblyopia and found a slightly thicker central macular region and 6-mm ring area thicknesses and RNFLT in amblyopic compared with normal eyes.

Keywords: amblyopia, macular thickness, retinal nerve fiber layer

ÖZ

Amaç: Bu çalışmanın amacı maküler ve peripapiller retina sinir lifi tabakası kalınlığı ile ambliyopi arasındaki ilişkiyi araştırmak.

Gereç-Yöntem: Bu çalışmada hipermetropik anizometropik ambliyopisi olan toplam 56 çocuk hasta değerlendirildi. Kontrol grubu olarak hastaların sağlam gözleri kullanıldı. Snellen eşeli (analiz için logMAR'a dönüştürülmüş) ile en iyi düzeltilmiş görme keskinliği, yarık lamba muayenesi, fundus muayenesi, örtme ve örtme-açma testi ve göz hareketleri dahil olmak üzere kapsamlı göz muayenesi yapıldı. Her iki gözün maküler kalınlığı, retinal sinir lifi tabakası kalınlığı(RNFLT), aksiyel uzunluğu ve optik disk çapı ölçüldü.

Bulgular: Ortalama yaş 7.25±1.89 yıl idi. Ambliyopik ve sağlam gözler için ortalama en iyi düzeltilmiş görme keskinliği sırasıyla 0.33 ± 0.20 logMAR ve 0.0 ± 0.0 logMAR idi. Makula merkez kalınlıkları ambliyopik ve sağlam gözlerde sırasıyla 225,55 ± 18,86 µm ve 215,7 ± 12,96 µm idi. Makula 6 mm dairesel alan kalınlıkları ambliyopik ve sağlam gözlerde sırasıyla 281,32±33,51 µm ve 256,07±28,91 µm idi. RNFLT ambliyopik ve sağlam gözlerde sırasıyla 281,32±33,51 µm ve 256,07±28,91 µm idi. RNFLT ambliyopik ve sağlam gözlerde sırasıyla 108,39 ± 11,59 µm ve 104,61 ± 8,43 µm idi. Maküler merkez kalınlığında, maküler 6 mm dairesel alan kalınlığında ve RNFLT'de ambliyopik ve sağlam göz arasında istatistiksel anlamlı farklılık saptandı(p<0.05). Ambliyopik gözlerin görme keskinliği ile maküler kalınlık ve RNFLT arasında pozitif korelasyon vardı.

Sonuçlar: Bu çalışmada ambliyopide objektif olarak ölçülen retina değişiklikleri araştırıldı ve maküler kalınlık ve RNFLT normal gözlere göre ambliyopik gözlerde daha kalın bulundu.

Anahtar kelimeler: amliyopi, maküler kalınlık, retina sinir lifi tabakası

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INTRODUCTION

Amblyopia is reduced best-corrected visual acuity in one or both eyes caused by abnormal visual experience during visual development. Causes of amblyopia are strabismus, anisometropia, and form-vision deprivation.¹ Each of these has functional and morphologic effects on the visual cortex and lateral geniculate nucleus.² Although amblyopia is associated with a structurally normal eye, several studies have reported visual field abnormalities and anatomical changes in visual pathways of amblyopic patients.³⁻⁶ It has been hypothesized that amblyopia may affect the postnatal maturation of the retina, including the postnatal reduction of retinal ganglion cells, which would lead to a measurable increase in retinal nerve fiber layer thickness (RNFLT) in amblyopic eyes.⁷ Some investigators have found an increased RNFLT in amblyopic eyes, whereas others have found no significant differences.8-11 Studies of macular thickness have also produced discordant results.¹²⁻¹⁶

This study examined the relationship between macular and peripapillary RNFL thickness and amblyopia of children aged 4 and 13 years.

SUBJECT AND METHODS

This study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Bagcilar Training and Research Hospital Clinical Research Ethics Committee. Written informed consent was obtained from the parents or legal guardian of each patient following a detailed explanation of the study objectives and protocol. A total of 56 pediatric patients(20 females, 36 males), which followed up at Health of Sciences University Bagcilar Training and Research Hospital Eye Clinic, with hyperopic anisometropic amblyopia were evaluated in this study. They were still in patching treatment for amblyopia. As the control group, we used the patients' fellow eyes. Inclusion criteria were the presence of unilateral amblyopia due to hyperopic anisometropia for the children in the amblyopia group. Presence of strabismus, nystagmus, deprivation amblyopia, history of previous ocular surgery, intraocular inflammation, corneal disease, retinal disease or optic nerve disease, ocular media opacities, including cataract or other diseases of the visual pathway, glaucoma, neurological disease, and insufficient cooperation were exclusion criteria. All refractive errors were converted to spherical equivalent values. Anisometropia was defined as a 1.50 diopter(D) difference between two eyes. Unilateral amblyopia was defined as best-corrected visual acuity of 0.20 LogMAR or worse in one eye and at least a 2-line difference between the amblyopic eye and the fellow eye.

Study Parameters

A comprehensive eye examination was performed, including best-corrected visual acuity with Snellen charts (converted to logMAR for analysis), slit-lamp examination, fundus examination, cover and, coveruncover testing, and ocular motility testing. Three drops of cyclopentolate hydrochloride 1% were administered 5 minutes apart, and autorefraction was performed using an automatic refractor-keratometer device (Canon, Tokyo, Japan) approximately 45 minutes after the last drop.

Imaging

Optical coherence tomography (Nidek RS-3000) was performed through dilated pupils to obtain cross-sectional measurements of the retina. This instrument used partial coherence interferometry technology to obtain optical A-scans of the retina. Retinal boundaries used to make these measurements were identified by changes in reflectivity associated with these interfaces. This instrument has an axial resolution of approximately 10 micrometers(µm).¹⁷⁻²¹ Peripapillary RNFL thickness was measured using the "fast RNFL thickness" scan protocol. This comprised 256 sampling points along a circular scan path. Three scans were performed, and the average was used in analyses. This is a measure of the total cross-sectional area of ganglion cell axons converging toward the optic disc. Macular thickness was measured as the distance between the internal limiting membrane and the retinal pigment epithelium using the "fast macular scan" protocol. The macular retinal thickness of both eyes at the center and 1-, 3-, and 6-mm rings in different segments (superior, inferior, nasal, and temporal) were measured. An average of 5 scans was used in the analysis. A single experienced operator performed all scans.

Statistical Analysis

In this study, statistical analysis was done by the NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) pocket program. In

the evaluation of data, repeated statistical methods (mean, standard deviation) as well as paired t-test for comparison of amblyopic and fellow eyes, variance analysis of multiple groups, Pearson correlation test for the relationship between variables, were used. The results were evaluated at p<0.05 level.

RESULTS

The mean age was 7,25±1,89 years(4-13 years). For the amblyopic and fellow eyes, the mean best-corrected visual acuity was 0,33± 0,20 logMAR an, 0,0± 0,0 logMAR, the mean spherical equivalent refraction was 5,27±1,39 and 1,09±0,69 D, and the mean axial length were 21,4±0,71 and 22,1±0,37 mm respectively(p<0,05). Macular center thicknesses were 225,55±18,86 µm and 215,7±12,96 µm in amblyopic and fellow eyes, respectively(p<0,05). Macular 6mm ring thicknesses were 281,32±33,51 μm and 256,07±28,91 μm in amblyopic and fellow eyes, respectively(p<0,05). RNFLT were108,39±11,59 μm and 104,61±8,43 μm in amblyopic and fellow eyes, respectively(p<0,05). Optic disc area were 2,68±0.83 mm and 2,90±0,69 mm in amblyopic and fellow eyes, respectively(p<0,05). There was a statistically significant difference in the macular center thickness, in macular 6-mm ring area thickness and, RNFLT(p<0,05) (Table 1). There was a positive correlation between spherical equivalence of amblyopic eyes and macular thickness, RNFLT, and optic disc area; and a negative correlation between axial length.

DISCUSSION

In our study, we found statistically significant differences in macular thickness between amblyopic and non-amblyopic eyes, as measured by optical coherence tomography. Macular thickness was greater (by ~ 10 μ m) in the amblyopic than the normal fellow eye(p<0.05). Huynh et al¹² compared macular thickness between amblyopic and normal fellow eyes of 4118 children in a population-based study and found that macular thickness was 5-10 μ m greater in amblyopic eyes. Altindag et al¹³ also found that the macular thickness was significantly higher in strabismic amblyopic cases compared to the controls, similar to our study. Altintas et al¹⁰ found no differences in macular thickness between amblyopic and normal eyes. Rajavi et al¹⁵ found a significant difference in

	Amblyopic Eye	Fellow Eye	р
VA(logMar)	0,33±0,20	0,0±0	0,0001
Macula center (micron)	225,55±18,86	215,7±12,96	0,0001
Macula 6-mm ring area (micron)	281,32±33,51	256,07±28,91	0,0001
RNLFT (micron)	108,39±11,59	104,61±8,43	0,004
AxL (mm)	21,4±0,71	22,1±0,37	0,01
Optic Disc Area (mm)	2,68±0,83	2,90±0,69	0,004

Values are presented as mean±standard deviation VA:Visual Acuity, mm:milimeter, RNFLT: Retinal Nerve Fiber Layer Thickness, AxL: Axial Length

Table 1: Comparison of amblyopic eye and fellow eye for Visual Acuity, Macula center thickness, Macula 6-mm area thickness, RNFLT, Axial Length, and Optic Disc Area

macular retinal thickness at the center and 1-mm ring area in the moderately to severely amblyopic eyes compared to the non-amblyopic controls, whereas this difference was not observed at the 3and 6-mm rings. We found in the macular center and also in the 6-mm ring area statistically significant differences. Liu et al²² measured a mean retinal thickness of 201.5±17.9 and 176.7±14.8 µm at the central and foveal areas in refractory amblyopic eyes, respectively, and they also found a significant difference when compared with normal Chinese children. Andalib et al²³ reported a significantly higher macular thickness in anisometropic amblyopic cases, though they did not find the same result in strabismic amblyopic cases. Doguizi et al²⁴ reported too significantly higher central macular thickness in amblyopic eyes than in fellow and control eyes(249.6±12.8, 244.1±14.9, and 243.1±12.6 respectively), but they found no significant difference between groups in terms of inner and outer macular thickness. Taşkıran-Çömez et al did not found in macular thickness significant difference in their series including myopic and hyperopic amblyopic children.

In the present study, we found RNFLT was~4 μ m thicker in amblyopic eyes, and that was statistically a significant difference (p<0.05). Repka et al¹¹ found that amblyopic eyes have ~ 7 μ m greater thickness for RNFLT. Altintas et al¹⁰ found RNFLT 2.5 μ m thicker in amblyopic eyes, and that was not significant in their

study. Bozkurt et al²⁵ also used a scanning laser polarimeter to examine 24 children with anisometropic amblyopia and found no difference in all parameters. Colen et al²⁶, using a scanning laser polarimeter, reported similar findings in 20 subjects with unilateral strabismic amblyopia. Baddini-Caramelli et al²⁷, using a scanning laser polarimeter in 21 children with unilateral amblyopia, found that the RNFLT may be thicker in amblyopic eyes. Yen et al7, examined 38 children with unilateral amblyopia (20 strabismic, 18 refractive) and found that children with refractive amblyopia had significantly greater average RNFLT in the amblyopic eye than the normal fellow eye, but no differences were found in children with unilateral strabismic amblyopia. Yoon et al²⁸, found that children with anisometropic amblyopia had greater average RNFLT in their amblyopic eyes than normal fellow eyes. Taşkıran-Çömez et al²⁹ did not found in RNFLT significant difference in their series including myopic and hyperopic amblyopic children.

The optic disc area is directly associated with the number of nerve fibers in the optic nerve. Small hyperopic eyes may have a small retinal surface and smaller optic disc. A deficiency of nerve fibers may be responsible for decreased visual acuity in amblyopic eyes.^{30,31} Some studies have shown that eyes with amblyopia may have smaller optic disc areas than non-amblyopic eyes and healthy control eyes, and subclinical optic disc anomalies may be associated with amblyopia; some did not found any difference.^{7,29,32} Be that as it may, the relationship between amblyopia and disc anomalies is questionable; the recently announced small disc area related to amblyopia may have been brought about by a connection with hyperopia and anisometropia, and not due to a direct causal relationship between small disc area and amblyopia.³³ The present study found a significant difference between amblyopic and fellow eyes.

These inconsistent findings may be explained in part by the use of different instruments, the relatively small sample sizes, and the lack of population-based controls in all the studies. Yen et al⁷ hypothesized that the normal postnatal reduction (apoptosis) of retinal ganglion cells is arrested in amblyopia and predicted that this would cause increased RNFL thickness. The arrest of normal postnatal changes would likely result not only in increased RNFL thickness but also would affect the normal maturation of the macula, including the movement of Henle's fibers away from the foveola and a decrease in foveal cone-diameter. This would result in increased foveal thickness. Our findings were similar to the Yen's hypothesis. The increased central macular and foveal minimum thickness in amblyopic eyes could account for part of the reduced VA observed. It is not clear whether the change in central macular and foveal minimum thickness preceded the development of amblyopia or occurred afterward.

In conclusion, this study found a slightly thicker central macular region and 6-mm ring area thicknesses and RNFLT in amblyopic eyes compared with normal fellow eyes, using optical coherence tomography. Further research should aim to study the effect of foveal thickness changes on visual acuity in amblyopic children.

Ethics Committee Approval: Bağcılar Training and Research Hospital Clinical Research Ethics Committee approval was obtained. (2016/489). Conflict of Interest: No. Funding: No. Informed Consent: Yes.

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