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Original Article

Evaluation of retinal nerve fiber layer thickness using optical coherence tomography in unilateral anisometropic amblyopic patients

Tek taraflı anizometropik ambliyopik hastalarda optik koherens tomografiyi kullanarak retina sinir lifi tabakası kalınlığının değerlendirilmesi

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ABSTRACT

Aim: To evaluate the retinal nerve fiber layer (RNFL) thickness in cases with unilateral anisometropic amblyopia using optical coherence tomography (OCT).

Material and Method: Retrospective cross–sectional observational case series. OCT of the peripapillary RNFL thickness of amblyopic and fellow eyes was performed in 35 patients age 6 to 63 years (mean 28.91±15.45) with unilateral anisometropic amblyopia. All OCT scans were performed within three session by the same operator with cyclopentolate pupil dilatation for the best correct result. Scans with signal strength more than 7 (on a 10-point scale) were considered acceptable and included in the analysis only. Statistical analysis of retinal thickness differences between the amblyopic and healthy (fellow) eyes were determined using the independent samples T-test. Additionally it was utilized from Pearson correlation test to establish the correlation between RNFL values and refractive disorder levels.

Results: While the average RNFL thickness was measured 93.91±17.18 micrometer in amblyopic eyes; that was measured 94.51±14.54 micrometer in fellow eyes. There was no statistically significant difference between the RNFL thickness of the amblyopic eyes and healthy fellow eyes.

Conclusion: In cases with anisometropic amblyopia, RNFL thickness measurements between amblyopic and healthy eyes were similar in general.

Keywords: anisometropic amblyopia, optical coherence tomography, retinal nerve fiber layer

ÖZ

Amaç: Tek taraflı anizometropik ambliyopi olgularında optik koherens tomografi (OKT) kullanılarak retinal sinir lifi tabakası (RSLT) kalınlığını değerlendirmek.

Gereç ve Yöntem: Retrospektif kesitsel gözlemsel olgu serileri. Tek taraflı anizometropik ambliyopisi olan yaşları 6 ile 63 yıl aralığındaki (ortalama 28,91±15,45) 35 hastanın ambliyopik ve sağlıklı gözlerinin peripapiller RSLT kalınlığı OKT ile ölçüldü. Tüm OKT taramaları, en doğru sonucu elde edebilmek için aynı operatör tarafından ve siklopentolat pupil dilatasyonu birlikteliğinde üç seansta gerçekleştirildi. Sadece, sinyal gücü 7'den fazla olan (10 noktalı bir ölçekte) taramalar çalışma kapsamına alındı ve analize dahil edildi. Ambliyopik ve sağlıklı (diğer) gözler arasındaki retinal kalınlık farklılıklarının istatistiksel analizi, bağımsız örneklem T testi kullanılarak belirlenmiştir. Ayrıca, RSLT değerleri ve refraktif bozukluk seviyeleri arasındaki korelasyonu belirlemek için Pearson korelasyon testinden yararlanılmıştır.

Bulgular: Ambliyopik gözlerde ortalama RSLT kalınlığı 93,91±17,18 mikrometre olarak ölçüldü; diğer gözlerde 94,51±14,54 mikrometre ölçüldü. Ambliyopik gözlerin RSLT kalınlığı ile sağlıklı gözlerin gözleri arasında istatistiksel olarak anlamlı bir fark yoktu.

Sonuç: Anizometropik ambliyopisi olan olgularda ambliyopik ve sağlıklı gözler arasındaki RSLT kalınlığı ölçümleri genel olarak benzerdi.

Anahtar kelimeler: anizometropik ambliyopi, optik koherens tomografi, retina sinir lifi tabakası

INTRODUCTION

The visual process consists of a series of neural transmissions continuing from the lateral geniculate nucleus to the striate cortex. The visual process is in occipital lobe's calcarine sulcus Broadmann area 17. Inhibitory and excitatory binocular convergence comes into play in this part [1]. Through cortical synaptic connections, a fragmented representation of a scene or object is integrated. Thus, a perceptible visual perception occurs [2]. Parvocellular cells in the ventral tract of the temporal lobe provide color and shape perception. Magnocellular cells of the dorsal pathway in the parietal lobe are responsible for localization and motion processing [3]. Amblyopia is an important cause of low visual acuity. It is thought to affect between 2% to 6% of the population [4]. Furthermore, amblyopia is a disease that is characterized with an abnormal contrast sensitivity and visual acuity (VA) in either one or two eyes. The reason is thought to be either abnormal binocular interactions or visual deprivation [5] which cannot be improved by refractive correction or accounted for by clinically determined anatomic defects of the eye or visual pathway [6]. Amblyopia is also associated with the loss of Snellen and grating acuity [7, 8] and deteriorations of the stimulus [9]. The pathophysiologic mechanisms of amblyopia were not elucidated. Strabismus, anisometropia and form–vision deprivation are considered to be classic causes of amblyopia [6]. It is believed that each of these result in amblyopia as a result of functional and morphological effects on the lateral geniculate nucleus and the visual cortex [10, 12]. It has been thought that the retinal maturation in the postnatal period may be influenced by amblyopia [13]. The retinal ganglion cell reduction is observed in the retinal maturation process during the postnatal period. This can cause a finite increase in the retinal nerve fiber layer (RNFL) thickness in patients with amblyopic eyes. Optical coherence tomography (OCT) is an imaging technique and it is a rapid and non–invasive technique Retinal structures (such as determination of the thickness of the peripapillary RNFL) can be objectively quantified by using this technique [14 - 17]. In the study, the aim is to show the difference between the amblyopic and fellow eyes in terms of the peripapillary RNFL thicknesses which were measured by using OCT in patients with a unilateral anisometropic amblyopia.

MATERIAL AND METHOD

Study Design: This comparative study was descriptive, retrospective, single center, which was performed from January 2013 to May 2013. In this study, patients who have undergone any eye surgery, ocular motility dysfunction, strabismus, amblyopia other than anisometropic amblyopia, lesions which cause visual loss in anterior segment and fundus examination, neurological disease, nystagmus, familial or self-glaucoma histories, optic nerve pathology (optical pit, tilted disc, etc.), retinal vascular diseases or macular diseases, peripapillary choroidal atrophy were excluded (n=8) from the scope of the study. This study is limited to 35 patients between 6 and 63 years of age. Unilateral anisometropic amblyopia was observed in Aamblyopic patients (n=35, between the ages of 6 and 63) and OCT was used to measure the nerve fiber layer of retina cells in both amblyopic and normal eyes. Research of differentiation was not conducted between young and old groups. Patients were recruited from the ophthalmology clinic of Turkey Republic Health Ministry and Sakarya University Medical School, Training and Research Hospital located in Turkey. This study was conducted in line with the Declaration of Helsinki and Sakarya University Medical School institutional board committee approved the study (No: 71522473.050.01.04/59). Informed consents each participant and their parents were obtained. Unilateral anisometropic amblyopia was the best corrected VA (BCVA) when there was at least a two–line difference between the normal and amblyopic eyes on the Snellen visual acuity charts and an interocular difference in refraction spherical equivalent of more than 2.0 diopters or cylindrical equivalent of more than 1.0 diopters [18]. Medical inspection included visual acuity testing, pneumotonometry, cycloplegic refraction, slit lamp examinations of the anterior segment, cover test, fundoscopy, cover-uncover test, fixation test, extraocular movements, duction and version testing. Patients with neurological diseases, nystagmus, glaucoma, intraocular pressure above 21 mm Hg, according to automated pneumotonometer (Canon TX–F), retinal disorders, optic disc pathology, strabismus, eccentiric fixation, inappropriate to OCT examination, ocular motility disorders, ophthalmic surgery or other visual pathway diseases were excluded from the study. The same examiner performed the measurement. Pupils were dilated five minutes apart with 1% cyclopentolate HCl for three times before the examination. Sciascopic and autorefractive (Topcon KR–8100) measurements were recorded 45 minutes after the last instillation of 1% cyclopentolate HCl drop. Meantime cycloplegic effect continued, detailed anterior segment examination, indirect fundoscopy and OCT [(OCT-4000) (Zeiss Cirrus HD OCT) Carl Zeiss Meditec, Inc., CA)] scanning of RNFL thickness measurements were verified. One week later, best corrected visual acuity was determined according to these refractive measurement records for both eyes. BCVA of the patients was measured 0.9 units or more in healthy eyes and 0.3 – 0.5 units in amblyopic eyes according to Snellen Chart. peripapillary retinal nerve fiber layer thickness was measured via performing circular scans around the optic disc. External fixation was done for the scanning of the optic disc. A single skilled technician took multiple images (minimum 3 images) from eyes. Scans which had signal strength < 8 (on a 10-point scale) were not included in the study. On the other hand, the image with best signal strength was included in the analysis and it was considered acceptable. Low-coherence interferometry was done by using Cirrus HD-OCT 4000 device with the help of an 840 – nm superluminescent light – emitting diode. Thus, high – resolution tomograms was produced. It was used to scan the optic disc and the thickness of the RNFL. After pupil dilatation, "Optic Disc Cube 200 x 200" protocol was used to acquire data for optic disc parameters and a 6 – mm square grid can be scanned by using this protocol via acquiring 200 horizontal scan lines. There were 200 A-scans for each of these lines. Image analysis was done by using the version 5.0 Cirrus HD–OCT software. RNFL thickness was calculated for the entire cube by using layer – seeking algorithms. All 256 specific A–scans are in a center of the optic disc and in a 3.46 mm diameter circle. An average RNFL thickness and data in clock hours and quadrants were obtained by extracting them. Technician can sometimes assume that the circle eccentrically located. In this case, the circle was manually located in the center of the optic disc and then the data was analyzed. In this study, results of measurements were obtained in micrometer (μm) for all areas of all eyes, such as average RNFL thickness and four quadrants (nasal, inferior, temporal, superior).

Statistical Analysis: The results were analyzed statistically by using SPSS version 14.01 package program. The Kolmogorov-Smirnov test was used to evaluate whether or not the data were normally distributed. We used independent samples t – test to determine the statistical analysis of retinal thickness differences between the healthy and amblyopic eyes. Additionally, it was utilized for Pearson Correlation Test to establish the correlation between RNFL values and refractive disorder levels. Statistical significance was accepted when the p values was less than 0.05.

RESULTS

In this study, 70 eyes of 35 patients with unilateral anisometropic amblyopia were examined. Totally 21 (60%) males and 14 (40%) females were included in the study (**Figure 1**). Patients mean age was 28.91±15.45 years (age range 6–63 years), and the median was 29 years. Among patients diagnosed with anisometropia; there was a hyperopia in 13 (37.1%) cases, myopia was noticed in 2 (5.7%) cases, astigmatism (meridional) was noted in 15 (42.9%) cases and mixed type was noted in 5 (14.3%) cases (**Table 1**). Among 35 examined anisometropic ambliyopic eyes, 16 (45.7%) of them were right (Male/Female ratio: 9/7) and 19 (54.3 %) of them were left eye (Male/Female ratio:

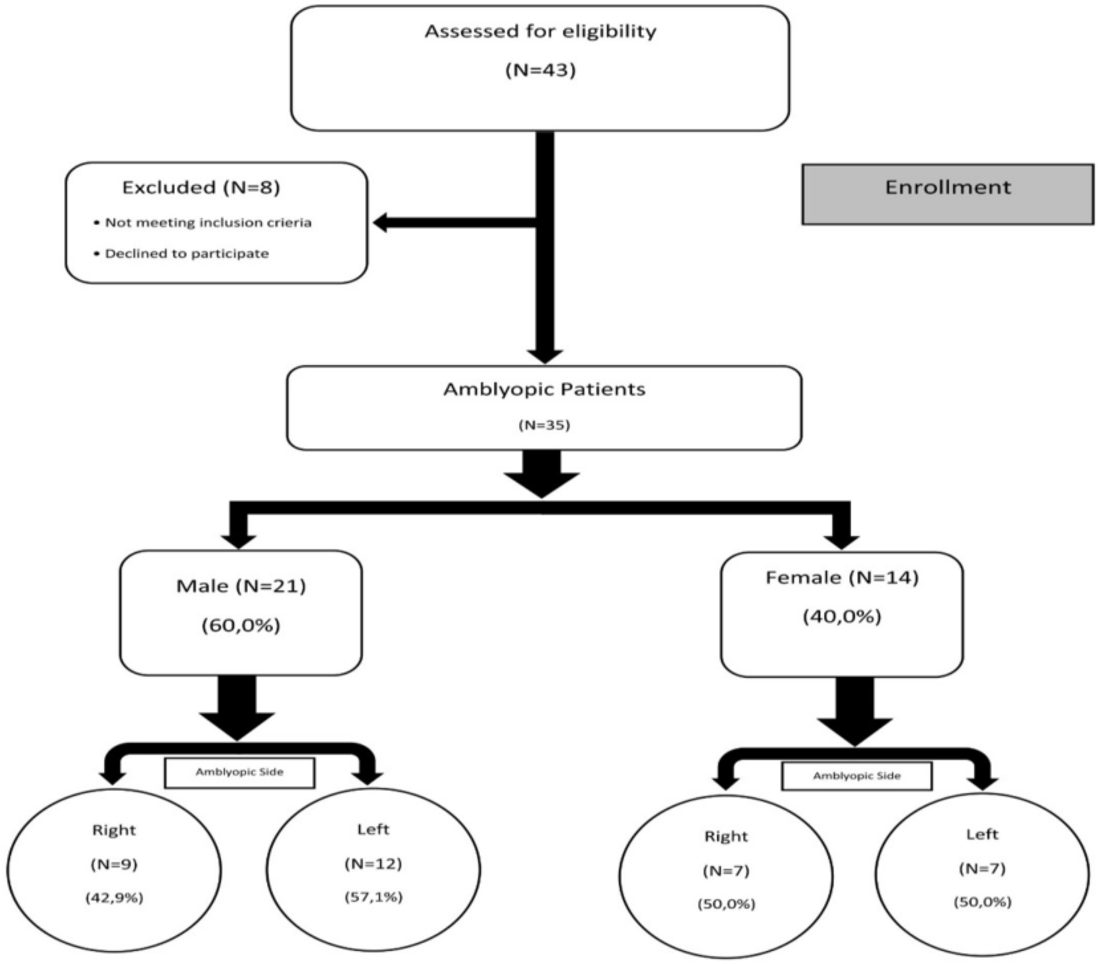

Figure 1. Flowchart of the study

Table 1. Distributions of amblyopic eyes by type of anisometropia

	n	%
Astigmatism	15	42.9
Hm*	13	37.1
Hm + Astigmatism	3	8.6
Myopia	2	5.7
Miyopia + Astigmatism	2	5.7
Total	35	100

**Hm:Hypermetropia*

12/7) (**Figure 1**). The mean total RNFL thickness was measured 94.51 micrometer in healthy fellow eyes and 93.91 micrometer in amblyopic eyes. According to our findings, no statistically significant difference was observed between them. It was also compared between any of four quadrants (superior, inferior, temporal, nasal) for both amblyopic and healthy fellow eyes (**Table 2**). BCVA was determined as 0.9 (97.70%) in healthy fellow eyes and 0.4 (41.57%) in amblyopic eyes. No relationship was determined between RNFL thickness itself and BCVA in the amblyopic eyes (r=-0.061) (p=0.729). However, there was no significant relationship between RNFL thickness values and refractive errors in the amblyopic eyes (r=0.137) (p=0.434) in line with Pearson's correlation test (**Table 3**).

Table 2. Comparision of mean RNFL thickness between amblyopic and fellow eyes

		n	Arithmetic Mean(µm)	Std. Error	Std. Deviation	Median	Change Interval	p
RNLF	Amblyopic	35	93.91	2.89	17.08	95.00	85	0.875
	Fellow	35	94.51	2.46	14.54	95.00	82	
Superior	Amblyopic	35	116.37	4.33	25.63	116.00	117	0.491
	Fellow	35	112.57	3.37	19.95	114.00	102	
Inferior	Amblyopic	35	123.9	4.47	26.42	126.00	142	0.46
	Fellow	35	128.06	3.39	20.06	128.00	108	
Temporal	Amblyopic	35	70.23	3.84	22.71	67.00	133	0.569
	Fellow	35	73.43	4.07	24.06	70.00	151	
Nasal	Amblyopic	35	75.63	2.99	17.67	73.00	70	0.277
	Fellow	35	71.77	1.86	11.03	73.00	44	

Table 3. Comparision of best corrected visual acuity (BCVA) between amblyopic and fellow eyes

		n	Arithmetic Mean (µm)	Std. Error	Std. Deviation	Median	Change Interval	p
BCVA	Amblyopic	35	0.415	0.04	0.22	0.40	0.65	<0.001*
	Fellow	35	0.977	0.01	0.06	1.00	0.20	

**p<0.05*

DISCUSSION

Amblyopia was previously thought to be an illness with a retinal abnormality. However, it was recently considered that amblyopia develops primarily due to the cerebral anatomical difference and transformation in the visual cortex lateral and the geniculate body [19]. According to Von Noorden et al. [20], it was shown that there was a reduction in the cellular sizes in parvocelluler layers which were enervated by the amblyopic eye in patients who were diagnosed with anisometropic amblyopia. Furthermore, this reduction was more marked in the lamina which included the crossed nerve fibers. According to animal experiments based study of amblyopia, the internal plexiform layer became thin and the nucleolar volume reduced in ganglion cell cytoplasms [21, 22]. Furthermore, it was specified that there was a decrease in the optic nerve size [23]. In a study that was conducted by Von Noorden et al. [24], an amblyopia was induced by using the unilateral lid suture in the Macaca mulatta. According to the results of the study, there was an arrest in the lateral geniculate body cell growth. An abnormal distribution of the cerebral cortex was observed and there was a reduction both in the density and size of the parafoveal ganglion cells It was indicated by Wiesel and Huble [25] that there was atrophy in the cerebral cortex neurons but they did not detect any influence on the retina. However, remarkable damages were observed in the visual cortex, the lateral geniculate body, and the ganglion cells were observed in the amblyopic eyes with visual deprivation amblyopia and strabismic amblyopia [26]. A significant decrease in the number and the size of the axons on the ganglion cells was observed as it was in the case of the thickness of the retinal nerve fiber layer. According to the study of Varma et al. [27] in which they examined 312 individuals with the mean age of 52 (age range: 40–79 years), measurements of total retinal nerve fiber layer thickness and temporal, superior, nasal, inferior quadrant thicknesses were performed by using OCT. Findings showed the thickness in the superior and the inferior quadrants and thinness in the nasal and temporal quadrants. Our results are similar to the findings of various studies [28, 29]. Visual abnormalities change because of different abnormal visual experiences and the age of onset. Children who are diagnosed with amblyopia and who have similar visual acuity may show distinct morphophysiologic variations and distinct visual functions. These anatomical and psychophysical differences can create greater and longer-lasting plasticity in some children and special treatment programs may be required in order to provide better therapeutic effectiveness. Therefore, it is not recommended to combine the patients with early- and late-onset amblyopia in studies [30]. In this study, there was no significant difference between the fellow and amblyopic eyes of anisometropic amblyopic patients in terms of the retinal nerve fiber layer thickness. Our findings are similar to the results of the previous OCT studies of amblyopia [31, 33]. There were some limitations. For instance, the study was a retrospective study with a small sample size. Furthermore, the measurement of SFCT was manually performed. Our OCT device did not have the software which should be used for the automated measurement of SFCT. Therefore, the distance from the hyperreective line of Bruch's membrane to the inner surface of the observed sclera under the fovea was manually measured [30].

Consequently, the retinal nerve fiber layer thickness measurements were similar in amblyopic eyes and fellow eyes of patients with anisometropic amblyopia. According to our results, it can be thought that peripapillary RNFL thickness values may not be significantly influenced by an anisometropic amblyopia process. However, retinal examinations with new modern instruments and postmortem histopatological studies in the near future may show the structural differences between anisometropic and normal eyes in terms of the retinal nerve fiber layer.

DECLARATION OF CONFLICT OF INTEREST

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