Survey of Nerve Fiber Layer Thickness in Anisometropic and Strabismic Amblyopia

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Abstract- To investigate the effect of anisometropic and strabismic amblyopia on the nerve fiber layer thickness. This cross-sectional study was done on 54 amblyopic subjects, equally in both strabismic and anisometropic groups. The thickness otonerve fiber layer measured in superior, inferior, nasal, temporal quadrants and as a whole in both eyes of both groups. The means of thickness were compared in amblyopic and sound eyes. In strabismus group, the average nerve fiber layer thickness of the sound eye , in superior, inferior, nasal and temporal quadrants and as a whole were 113.23±14, 117.37±25, 68.96±6, 69.55±14 and 93.40±8 microns respectively. In amblyopic eyes of the same group, these measurements were 103.11±18, 67.74±11, and 69.59±16 and 89.59±12 microns in superior, inferior, nasal, temporal quadrants and as whole respectively. In anisometropic groups, the sound eye measurements were as 130.96±22, 129.07±29, 80.62±12, and 83.88±20 and 107.7±13 microns in superior, inferior, nasal and temporal quadrants and as a whole orderly. In amblyopic eyes of this group the mean thicknesses were 115.63±29, 133.15±25, 78.8±15, 80.2±16 and 109.17±21 microns in superior, inferior, nasal, temporal quadrants and as a whole respectively. Statistically, there were no significant differences between amblyopic and sound eyes (P>0.5). Our study did not support any significant change in a nerve fiber layer thickness of amblyopic patients; however, decreased thickness in superior and nasal quadrants of strabismic amblyopia and except inferior quadrant and as a whole. These measurements may be a clue for management and prognosis of amblyopia in old age.

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Keywords: Anisometropic amblyopia; Strabismic amblyopia; Nerve fiber thickness

Introduction

Amblyopia is defined as a reduced best-corrected visual acuity in one or two eyes during the critical period of development without any structural defect. Some authors suggested that amblyopic eye may have an abnormality in afferent visual system anterior to the striate cortex such as the retina, retinal ganglion cell layer, nerve fiber layer, optic nerve and lateral geniculate bodies (1,2). Studies about visual deprivation amblyopia in animal showed histological changes in lateral geniculate bodies and cortex (3). Evidence for retinal changes in the amblyopic eye is controversial (2,4). It has suggested that amblyopia affects the retina, including the reduction of retinal ganglion cell, alteration in thickness of retinal nerve fiber layer (5). Some authors have reported increased nerve fiber layer thickness in amblyopic eye (4,5,6,8). On the other hand, other investigators showed no significant differences between the sound and amblyopic eyes (7,910,11). Peripapillary nerve fiber thickness, as a total measurement of both macular and peripheral nerve fiber layer thickness has reported being the best sign for assessment of optic nerve function. Due to some controversies on the effect of amblyopia on retinal nerve fiber layer thickness, we decided to measure the peripapillary retinal nerve fiber layer thickness in amblyopia and sound eyes of anisometropic and strabismic amblyopia subjects prospectively.

Materials and Methods

This cross-sectional study is a survey of nerve fiber layer thickness in strabismic and anisometropic amblyopic patients aged 10-20 years. This study approved by the ethics committees of the Guilan Medical Sciences University and was conducted according to the tenets of the declaration of Helsinki.

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Informed written consent was obtained from participants or their father in case of under 18-year-old. There was no conflict of interest.

Inclusion criteria

1-confirmed anisometropic amblyopia or monocular strabismic amblyopia

2-Aged 10-20 years

3- Visual acuity>of 20/200 (in both eyes)

4-No evidence of ocular disease

5-No evidence of central nervous system diseases

Patients' selection

According to the previous studies (4,5) and statistical estimation, the proper sample size was determined to be 54 cases (27 cases in each group. All selected patients, underwent complete eye examination including corrected and uncorrected visual acuities, Cycloplegic refraction with (refractions were done 45 minutes after instilling one drop of cyclopentolate 0.5%), alternate cover and prism test, and fundoscopy. The peripapillary nerve fiber layer thickness measured as an average and in four quadrants of superior, inferior, nasal and temporal in both eyes of patients using optical coherence tomography (OCT, Cirrous, Zeiss).We used the rapid retinal nerve fiber layer RNFL Scan. In this technique, three circular scans are taken around the disk with the diameter of 3.44. The instrument calculates the mean thickness of three scans for each quadrant (superior, inferior, nasal and temporal) and the RNFL as a whole. Measurements value with signal strength equal or more than eight are acceptable. In both groups descriptive statistics were calculated for initial and best-corrected visual acuities (BCVA), Cycloplegic refraction, and mean of RNFL thickness as a whole and in four quadrants in sound and amblyopic eyes and mean of differences of RNFL measurements.

Statistical analysis

The normal distribution of data was confirmed by Kolmogorov-Smirnov test. Independent *t*-test was used for comparison of measurements between two groups and dependent *t*-test for comparison of variables into each group between both eyes). We considered the RNFL thickness as the dependent variable and subjects as the independent variables. Independent *t*-test was used for comparison of measurements between two groups and dependent *t*-test for comparison of variables into each group between both eyes.

Results

Altogether, the mean age of participants was 13.2 3 years. About thirty of them were female (55.5%) and the remainder was male. We evaluated patients into groups.

Strabismic amblyopia

In this group, total subjects were 27 cases and 13 cases were male and the remainder was female. The mean ages of all patients, male and female were 13, 13 and 14 years respectively. The right eye was amblyopic in 20 subjects. The average Cycloplegic refraction in sound and amblyopic eyes was +3.0±1.4 and +3.5±1.7 diopter in order. The mean BCVA of the sound and amblyopic eyes was 20/25 and 20/40 respectively. The mean thickness of RNFL of sound eyes was 93.40±8 microns that decreased to 89.59±12 in amblyopic eyes $P>0.5$). The mean thickness of RNFL of right and left sound eyes, were 93.28±9.3 and 93.45±7.68 microns respectively ($P>0.50$). Table 1 provides detailed measurements of all quadrants in both sound and amblyopic eyes. The mean thickness of RNFL of right and left amblyopic eyes were 90.05±13.21 and 88.28±12.228 microns respectively ($P>0.52$). As seen in table1, all measurements of RNFL thickness decreased in amblyopic eyes ($P>0.52$) except the mild increment in temporal quadrant ($P>0.6$) and no change in inferior quadrant ($P>0.9$).

Anisometropic group

Twenty seven subjects of anisometropic amblyopia with the mean age of 13.5±3 years enrolled into the study. Six cases were female and the remainder was male. The right eyes were amblyopic in twelve patients. The mean cycloplegic refraction in sound and amblyopic eyes was 2.7±3.2 and 3.6±5.8 diopter respectively. The mean BCVA in sound and amblyopic eyes were 20/25 and 20/50 orderly. The mean thicknesses of RNFL in sound eyes were 107.7±13 microns that increased to 109.17±21 microns in amblyopic eyes ($P>0.52$). The mean thickness of RNFL of right and left sound eyes were 107.13±10.74 and 107±15.87 micron respectively ($P>0.50$). The mean thickness of RNFL of right and left amblyopic eyes were 103.67±12.81 and 114.67±29.21 micron respectively ($P>0.47$). Table 1 provides detailed measurements of all quadrants in both sound and amblyopic eyes There is no significant difference between the measurements of sound and amblyopic eyes ($P>0.5$ for all measurements). Full data of measurements are presented in table2.

In this group, All above measurements were higher than mean RNFL thickness of strabismic amblyopia

P>0.52). There are no significant differences between the measurements of sound and amblyopic eyes between two groups (*P*>0.5) for all measurements). In amblyopic eyes, all measurements of RNFL thickness decreased except mild increment in average RNFL and inferior quadrant as compared to sound eyes.

We observed thick RNFL in inferior quadrant of the strabismic amblyopia eye and superior quadrant of anisometropic amblyopic eye. In both groups, the thin RNFL thickness observed in the nasal quadrant. The normal eyes revealed the same data.

Table1. Retinal nerve fiber layer thickness (micron) in strabismic amblyopia

	Eye	Average thickness	Superior	Inferior	Nasal	Temporal	*P*.value
Sound eye	**Right**	93.28±9.34	116.29±14.14	124.86±28.85	65.28±5.28	74±16.38	0.52
	Left	93.45±7.68	112.15±14.35	114.75±22.37	70.25±8.06	65.3±11.47	
	Average	93.40±8	113.23±14	117.37±25	68.98±6	69.55±14	
***P*.value**		0.50	0.51	0.52	0.47	0.53	
Amblyopic eye	**Right**	90.05±13.21	105.7±1195	115.95+28.46	68.65±15.58	66.05±16.43	
	Left	88.28±12.22	95.57±29.92	121.43±20.86	65.14±7.62	72±16.5	
	Average	89.56±12	103.11±18	117.37±24	67.74±11	69.59±16	
***P*.value**		0.52	0.58	0.47	0.53	0.45	

Table 2. Retinal nerve fiber layer thickness (micron) in anisometropic amblyopia

	Eye	Average thickness	Superior	Inferior	Nasal	Temporal	*P*.value
Sound eye	**Right**	107.13±10.74	124.93±14.19	135.4±13.58	81.33±12.89	82.46±19.33	0.52
	Left	107±15.87	138.5±31.23	121.17±44.53	79.75±12.73	85.66±22.14	
	Average	107.7±13	130.96±22	129.07±29	80.62±12	83.21±16	
***P*.value**		0.50	0.45	0.54	0.51	0.49	
Amblyopic eye	**Right**	103.67±1281	123.42+28.43	126.75±21.38	80.66±17.07	84.66±18.98	
	Left	114.67±29.21	109.40±30.95	138.27±39.77	77.33±12.89	76.66±25.18	
	Average	109.17±21	115.63±69	133.15±25	78.8±15	80.21±16	
***P*.value**		0.47	0.53	0.48	0.52	0.52	

Discussion

Our study was done in fifty-four subjects of anisometropic and strabismic amblyopia with equal cases.

Anisometropic amblyopia

The mean thickness of RNFL of sound eyes 107.07±13 microns that increased to 109.78±21 in amblyopic eyes. The mean thickness of RNFL in superior, inferior, nasal and temporal quadrants sound eyes were 130.96±22, 129.07±29, 80.62±12, and 83.88±20 micron that decreased to 115.63±69, 78.8±15 and 80.21±16 in superior, nasal and temporal quadrants respectively and mild increase to 133.15±25 in inferior quadrants. Yen and associates (5), examined 38 subjects of strabismic and anisometropic amblyopia with OCT/2000, found that RNFL was thicker in the amblyopic eye as compared to sound eye in anisometropic amblyopia, but not different in patients with strabismic amblyopia. Colen *et al.*, (6) measured RNFL thickness in strabismic amblyopia and reported no significant difference between amblyopic and sound eye. May-Yung *et al*., (7), using the OCT mod 2000 Carl Zeiss to measure RNFL in 38 patients with unilateral strabismic and refractive amblyopia, found no significant difference between strabismic amblyopia and sound eye, but the RNFL was thick in the eye with refractive amblyopia. Yoon *et al.,* (4), using OCT3000, found that children with anisometropic amblyopia had greater average RNFL thickness in amblyopia than the normal fellow eye. These results based on the increment of RNFL, were as the same of our findings.

Strabismic amblyopia

The mean thickness of RNFL of sound eyes was 93.40±8 micron that decreased to 89.59±12 in amblyopic eyes. The mean thickness of RNFL in superior, inferior, nasal and temporal quadrants sound eyes were 113.23±14, 117.37±25, 68.96±6, and 69.55±14 micron that decreased to 103.11±18, 67.74±11 in superior and nasal quadrants respectively and mild

increase to 69.59±16 in temporal **.**

In our study, we found a small (3.81±10), but not a significant difference in average RNFL thickness between amblyopic and sound eye in all quadrants and no changes in inferior quadrant. The mean thickness of RNFL in superior, inferior, nasal and temporal quadrants of right and left sound eyes were not different significantly (P>0.5).

Our study showed that mean of RNFL thickness in superior, nasal and temporal quadrants decreased 15.3±, 1.8±and 3.6±micron respectively, and increased in central and inferior quadrants. Ann (8) and associates in their study, using stratus OCT, found a small difference in RNFL thickness between the amblyopic and sound eye in anisometropic and strabismic amblyopia (small increment in the amblyopia eye). On the other hands, Altintus (9) found no significant difference in RNFL thickness, using the OCT 3000, between the amblyopia and sound eye of strabismic amblyopia. Huynh (10) in the Sydney children eye study, showed no any difference between amblyopic and sound eye. Repka (11) and associates in their study that was done in 17 amblyopic cases, showed that RNFL thickness of sound and amblyopic eyes were 109.2 and 104.2 microns respectively. The average difference was 5 micron that was not significant. According to the previous studies, it is evident that in some studies, RNFL was thicker in the amblyopic eye as compared to sound eye in anisometropic amblyopia, but there is no difference in strabismic amblyopia. On the other hand, some investigation showed that the there was no significant RNFL thickness between the amblyopic and sound eye. Andalib *et al*., (12) in their study in 50 patients with anisometropic and strabismic amblyopia showed that in the anisometropic group, the mean macular thickness was significantly increased in the amblyopic eyes (222.6±47.8 μm) versus the fellow eyes (205.6±33.3 μm) (P=0.002), although there was no significant difference observed when comparing with the peripapillary nerve fiber layer. There was no significant correlation of above-mentioned measurements in the strabismic group (P=0.07). Konuralp *et al.*, in their study that was done in 30 adults with anisometric amblyopia, showed no significant differences between amblyopic and sound eyes (13).

These inconsistent and variable findings may be explained by some reasons.1-different a version of OCT instruments 2-lack of population-based control 3-relative small sample size 4-variability of RNFL measurements in hyperopia and myopia.

Peripapillary RNFL thickness decreased with increasing distance from the optic disc. A constant scan circle diameter on the OCT protocol would be smaller on the retina of the hyperopic eye, resulting in scan being closer to the disc and thicker measured RNFL. The contrast results would be true for myopic eyes (10). There is several limitations of our study namely, the small number of patients, wide range of refractive errors, lack of control groups of normal children, lack of normative data for children with OCT using the RNFL analysis program; therefore the absolute thickness should not be considered normal even for sound eye, and the wide range of amblyopia (mild-severe).

Our study showed that in different types of amblyopia, the RNFL altered in different quadrants and in some types, but not in other quadrants and types. Therefore it is recommended to consider another study with large sample with matched subjects.

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