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Optical Coherence Tomography Measurement of Peripapillary Retinal Nerve Fiber Layer Thickness in Patients with Unilateral Amblyopic Eyes

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Abstract

Background: Amblyopia is unilateral or less commonly bilateral reduction of best corrected visual acuity that cannot be attributed directly to the effect of any structural abnormality of the eye or posterior visual pathway. Amblyopia caused by abnormal visual experience early in life resulting from one of the following: Strabismus, anisometropia or high bilateral refractive error or stimulus deprivation.it is responsible for more unilateral reduced vision of childhood onset than all other causes combined. It affect 2-6% of general population.

Aim of Study: To compare RNFL thickness between normal and amblyopic eyes by OCT technique to define any structural abnormality in amblyopic eye.

Materials and Method: A case control hospital-based study was performed at Al-Sadder Medical city, Al-Najaf city. A total of 30 patients (14 female with 16 male) in (11-40) years old, range 29 years, who were diagnosed with unilateral amblyopia, 10 of them with strabismic amblyopia and the others 20 patient with anisometropic amblyopia were included in this study for a period started on January, till September 2014.

Full ophthalmologic examination was performed for both eyes for all patients ,as the fellow eye taken as a control group, examination include: visual acuity and best corrected visual acuity (measured with snellen chart adjusted at 6 m), refraction ; slit lamp bio microscopy, intraocular pressure measurement using Air-buff tonometer (Topcon®), extraocular movement , dilated fundoscopic nation and oct examination for peripapillary retinal nerve fiber layer thickness.

Results: The study included 30 patient with unilateral amblyopic eyes (14 female and 16 male) 20 of them with anisometropic amblyopia and 10 with strabismic amblyopia. Mean age for patients with anisometropia was (24.8 years ± 9.7) with range of 29 years, Maximum 40 years and Minimum 11 years.

Mean age for patients with squint was (19.1 years ± 8.9) with range of 29 years, Maximum 39 years and Minimum 10 years. In our study we found that the superior and inferior peripapillary RNFL thickness in anisometropic amblyopic eyes are significantly thinner than the other normal eyes. While in strabismic amblyopia the inferior peripapillary RNFL thickness is significantly thinner than the other normal eyes.

Conclusion: Our results suggest that amblyopia seems to have a significant effect on the peripapillary RNFL thickness, in strabismic and anisometropic amblyopia.

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Introduction

Amblyopia is unilateral or less commonly bilateral reduction of best corrected visual acuity that cannot be attributed directly to the effect of any structural abnormality of the eye or posterior visual pathway [1].

Amblyopia caused by abnormal visual experience early in life resulting from one of the following: strabismus, anisometropia or high bilateral refractive error or stimulus deprivation [2,3]. It is responsible for more unilateral reduced vision of childhood onset than all other causes combined [4]. It affect 2-6% of general population [5,6].

Amblyopia is diagnosed In the absence of an organic lesion, (till now there is no structural changes in the amblyopic eye can be found to be helpful for diagnosis), a difference in best corrected visual acuity of two Snellen lines or more (or >1 log unit) is indicative of amblyopia. Visual acuity in amblyopia is usually better when reading single letters than letters in a row. This 'crowding' phenomenon occurs to a certain extent in normal individuals but is more marked in amblyopes and must be taken into account when testing preverbal children [7].

The neural sites that are influenced by visual deprivation are still under investigation. Nevertheless, it has been reported by several studies on humans and animals that, during the neonatal period, visual deprivation has an effect on the growth of cells in the lateral

geniculate body that receives input from the amblyopic eye and a shift in the dominance pattern in the visual cortex [8,9]. Amblyopia occurs during the period when the neuronal network between the retina and the cerebral cortex is developing and maturing. Thus this condition is frequently developed during the first 2-3 years of the postnatal period; however, it may be developed up to the age of 8–9 years. Amblyopia is curable if treated early [10].

During fetal development, there is a rapid decline in cell density in the retinal ganglion cell layer toward the end of gestation. In humans, the total population of cells in the ganglion cell layer is highest (2.2-2.5 million cells) between approximately weeks 18 and 30 of gestation [11]. After this, the cell population declines rapidly to (1.5-1.7 million cells). The number of axons in the human optic nerve also decreases during gestation .At 16-17 weeks of gestation; the estimated number of axons was 3.7 million. The number of axons in the human adult optic nerve is 1.1 million. If amblyopia affects the process of postnatal reduction of ganglion cells; RNFL thickness may be affected more than that in the normal eye [12].

Several techniques to evaluate the RNFLT, such as red-free ophthalmoscopy, scanning laser polarimetry (SLP) and optical coherence tomography (OCT) have been described [10]. OCT is a noninvasive, noncontact technique that measures RNFLT [13]. The RNFLT measured by OCT corresponds to the RNFLT measured histologically [14]. Because OCT is based on near-infrared interferometry, the thickness measurement is not affected by refractive status or axial length of the eye, or by light changes in nuclear sclerotic cataract density [15].

Aim of Study

To compare RNFL thickness between normal and amblyopic eyes by OCT technique looking for any structural abnormality in the amblyopic eye.

Materials and Methods

A case control hospital-based study was performed at Al-Sadder Medical city, Al-Najaf city. A total of 30 patients (14 female with 16male) in a (12-40) years old, range of 29 years, who were diagnosed with unilateral amblyopia, 10 of them with strabismic amblyopia and the others 20 patients with anisometropic amblyopia included in this study for a period started on January, till September 2014.

Since our research is intended to measure peripapillary retinal nerve fiber layer thickness of amblyopic eye as measured by OCT and compare it with the other normal fellow eye.

After taking informed consent from the patients, detailed history was obtained from each patient. Full ophthalmologic examination was performed for both eyes for all patients, as the fellow eye taken as a control group, examination include: visual acuity and best corrected visual acuity (measured with Snellen's chart adjusted at 6 m), refraction; slit lamp biomicroscopy, intraocular pressure measurement using Air-buff tonometer (Topcon®), extra ocular movement, dilated fundoscopic examination and oct examination for peripapillary retinal nerve fiber layer thickness. Patient with organic eye disease, history or evidence of intraocular surgery, those with myopic retinal degenerations, history of glaucoma, cataract, retinal disorders or laser treatment and patient not cooperative for oct examination were excluded from the study.

OCT technique

After obtaining informed consent, the pupils were dilated with1 drop of 1% tropicamid eye drop. RNFL thickness was measured 30 minute later. The oct system used in this study was oct model 2000 (3d oct, TOPCON, at AL.HAKEEM hospital) .To measure RNFL thickness, the examiner focused a scanning baem on the fundus with infrared sensing camera, RNFL 3.45 mm centered on optic disc area was used for RNFL thickness measurement for each eye.

In this study, measurements from total areas were obtained in micrometer units. Average superior, inferior, nasal and temporal RNFL thickness was detected by the circular scan. All OCT measurements were performed by the same technician. In every case, the right eye was always measured first, followed by the left eye.

Statistical Analysis

Data analyzed by SPSS version 20 {statistical package for social science version 20}.

Mean and standard deviation were used. T-test was used to compare between normal and amblyopic eyes, graphs used as needed. Result considered significant when p-value is equal or less than 0.05.

Results

At the end of this study, there were 30 patient with unilateral amblyopic eyes (14 female and 16 male) 20 of them with anisometropic amblyopia and 10 with strabismic amblyopia. Mean age for patients with anisometropia was (24.8 years ± 9.7) with range of 29 years, Maximum 40 years and Minimum 11 years.

Mean age for patients with squint was (19.1 years ± 8.9) with range of 29 years, Maximum 39 years and Minimum 10 years as shown in table 1.

Study showed that the superior and inferior peripapillary RNFL thickness in anisometropic amblyopic eyes are significantly thinner than the other normal eyes with p-value 0.02 and 0.03 respectively (Tables 2 and 3), while the nasal and temporal peripapillary RNFL thickness are not significant statistically with p-value more than 0.05, as shown in table 4.

While in strabismic amblyopia the inferior peripapillary RNFL

Table 1: General features of study sample.

Feature		No.	%
Age group	Less than 20	11	36.7
	20-30	12	40
	21-40	7	23.3
Total		30	100%
Gender	Male	16	53.3
	Female	14	46.7
Total		30	100%
Type of amblyopia	Anisometropia	20	66.7
	Squint	10	33.3
Total		30	100%
Occupation	Student t	15	50
	Free worker	9	30
	Housewife	5	16.7
	Teacher	1	3.3
Total		30	100%
Refractive error	Myopia	5	25
	Hypermetropia	13	65
	Hypermetropic	2	10
	Astigmatism		
Total		20	100%

Table 2: Basic clinical data for patient with anisometropic amblyopia.

Age	BCVA	Superior		Inferior		Nasal		Temporal	
		Normal	Amblyopic	Normal	Amblyopic	Normal	Amblyopic	Normal	Amblyopic
11	Jun-36	126	111	138	125	55	65	81	73
13	Jun-18	141	129	144	144	76	102	89	75
13	Jun-18	134	117	113	130	76	70	66	86
13	Jun-18	141	129	144	144	76	102	89	75
18	Jun-60	121	110	118	105	76	84	96	69
20	Jun-18	130	107	150	123	122	72	90	129
20	Jun-24	119	113	133	124	80	59	72	69
20	Jun-24	119	113	133	124	80	59	72	69
21	Jun-18	104	118	112	121	72	105	94	74
22	Jun-24	126	105	156	121	122	70	90	129
22	Jun-18	128	128	125	123	87	94	84	121
25	Jun-18	125	100	115	99	75	34	89	75
25	Jun-24	129	125	135	123	73	85	88	84
27	Jun-36	108	87	115	119	75	62	68	83
33	c.f 2m	134	143	131	33	51	71	62	55
35	c.f 1m	142	51	126	66	97	41	69	44
38	Jun-24	69	61	114	84	67	41	63	59
40	Jun-18	130	107	120	113	82	65	87	82
40	Jun-24	116	117	138	142	96	123	122	84
40	Jun-24	120	131	108	126	73	99	96	81

Table 3: Basic clinical data for patient with strabismic amblyopia.

Age	BCVA	Superior		Inferior		Nasal		Temporal	
		Normal	Amblyopic	Normal	Amblyopic	Normal	Amblyopic	Normal	Amblyopic
10	Jun-18	114	120	121	75	83	70	87	67
11	Jun-36	127	106	119	118	81	64	56	72
12	06-Dec	136	127	118	119	64	81	73	56
13	Jun-36	102	137	121	124	74	74	84	53
18	c.f 4m	147	115	113	117	73	85	145	65
19	Jun-24	121	97	111	99	68	25	88	79
20	c.f 1m	142	1	126	66	97	41	69	44
21	Jun-60	103	80	117	119	70	57	61	86
28	06-Dec	120	120	156	135	32	72	77	99
39	Jun-60	103	26	116	40	63	57	61	86

Table 4: Comparison by mean and SD between normal and amblyopic eyes for patients with anisometropia with p-value.

Peripapillary NFL quaderant	Normal eye (mean±SD)	Amblyopic eye (mean±SD)	P value
Superior	123.1±16.3	110.1±22.4	0.02
Inferior	128.4±13.9	114.5±26.9	0.03
Nasal	80.6±17.8	75.2±23.8	0.4
Temporal	83.4±14.6	77.4±27.7	0.4

Table 5: Comparison by mean and SD between normal and amblyopic eyes for patients with squint with p-value.

Peripapillary NFL quaderant	Normal eye (mean±SD)	Amblyopic eye (mean±SD)	P value
Superior	121.5±16.5	97.9±35.6	0.08
Inferior	121.8±12.7	101.2±30.7	0.05
Nasal	70.5±16.9	62.6±18.4	0.4
Temporal	80.1±25.5	70.7±17.1	0.4

thickness is significantly thinner than the other normal eyes with p-value 0.05 while the superior, nasal and temporal peripapillary RNFL thickness are not significantly different than the other normal eyes with p-value more than 0.05, as shown in table 5.

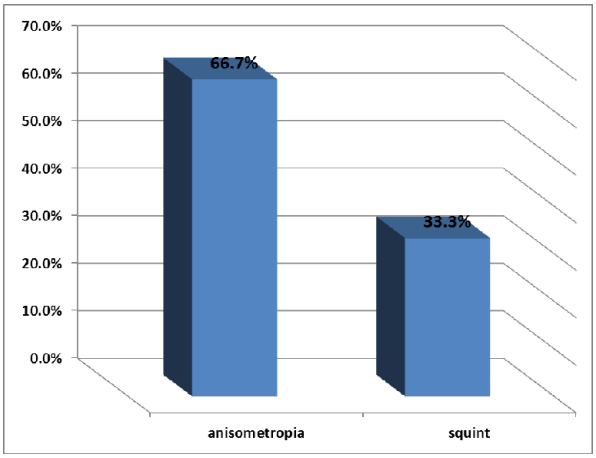

Figure 1: Distribution of study group according to type of amblyopia.

Discussion

Amblyopia may have different effects at various levels of the visual pathway. Receiving input from the amblyopic eye causing atrophy for the cells in the lateral geniculate nucleus has been reported. Several

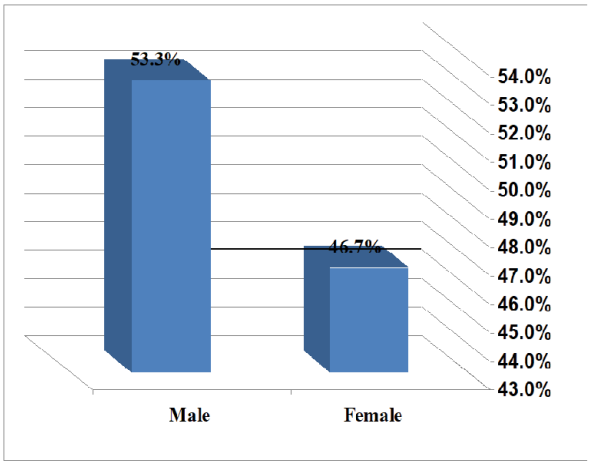

Figure 2: Distribution of study group according to gender.

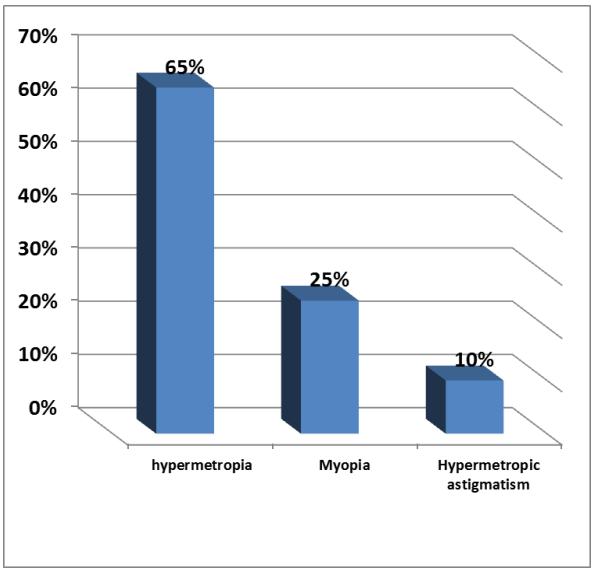

Figure 3: Distribution of the sample according to the refractive error.

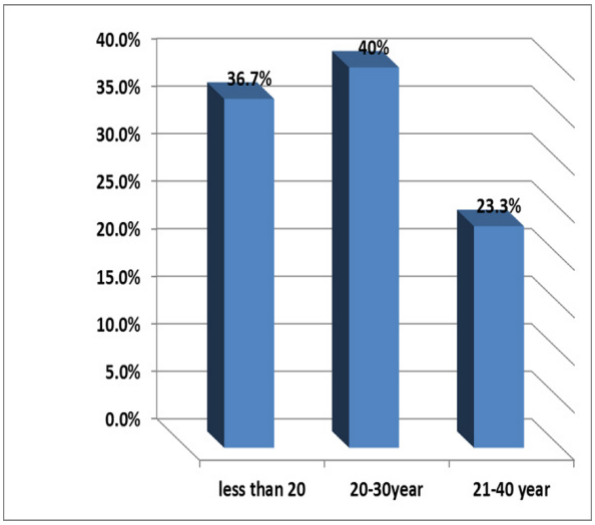

Figure 4: Distribution of the sample according to the age group.

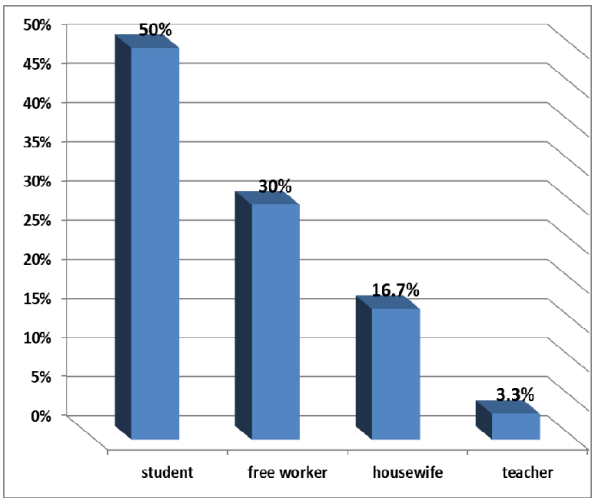

Figure 5: Distribution of study group according to occupation.

experiments have demonstrated that light deprivation can cause modifications of retinal ganglion cells, such as cell loss, mean nuclear volume diminution in ganglion cell cytoplasm, internal plexiform layer thinning in rats and cats, and reduction in optic nerve size area in mice [16-18].

In many studies, retinal changes were investigated using imaging devices. Several OCT studies have investigated the RNFL in amblyopia. OCT studies of RNFL thickness in amblyopia reported different findings [18].

Repka MX, et al. (2009) measured the thickness of the peripapillary RNFL in amblyopic and fellow eyes with OCT in anisometropic amblyopia [19]. They found no meaningful difference in the RNFL thickness. Altintas O, et al. (2005) reported that the RNFL thickness was 2.5μm thicker in amblyopic eyes but that this difference was not statistically significant in both types of amblyopia [20]. Study was done in Turkey by 21. Yuksel N, et al. published in 2005, the study reveal no statistical difference in peripapillary RNFL thickness between amblyopic and sound eye in both anisometropic and strabismic amblyopia [21]. A study was done by Dickman A, et al. in 2012 and concludes there is no difference in thickness in anisometropic amblyopia, while in strabismic amblyopia; the amblyopic eye was significantly thicker than the sound eyes [22]. Study was done by Abtaibi AG, et al. in ALRiyadh, Saudi Arabia in 2011and concluded that peripapillary RNFL thickness was significantly thicker in amblyopic eye than the sound eyes in anisometropic amblyopia while in strabismic amblyopia was not significantly different [23]. Dickman A, et al. study at 2011, was concluded that the amblyopic eyes was significantly thicker in amblyopic than sound eye in anisometropic but not in strabimic amblyopia [24].

Similarly, Yoon SW, et al. (2005) measured the macular and peripapillary RNFL in patients with anisometropic amblyopia. They reported that the RNFL in patients with amblyopia was significantly thicker [25].

Study done by Micheal X, et al. at 2006 and concluded that peripapillary RNFL thickness was slightly thinner than the sound eyes in both anisometropic and strabismic amblyopia [26]. Baddini-Caramelli C, et al. report study at 2001and concluded that there was slight decrease in peripapillary RNFL thickness in amblyopic eye than the sound eyes [27].

In this study we compared the global and four quadrants' RNFL thickness of amblyopic eye and other normal fellow eyes in anisometropic and strabismic amblyopia using SD-OCT (spectral domain optical coherence tomography).

We found statistically significant difference among the groups of anisometropic amblyopia in which the superior and inferior peripapillary RNFL thickness is significantly thinner than those of the normal fellow eyes with p-value 0.02, 0.03 respectively. While those of temporal and nasal peripapillary RNFL thickness are not statistically significant in which p- value more than 0.05.

In strabismic amblyopia the inferior peripapillary RNFL thickness is significantly thinner with p-value equal 0.05. While the superior, nasal and temporal peripapillary RNFL thicknesses are not significant statistically.

In this study, our result are in agreement with Micheal X, et al. (2006) [26] and with Baddini-Caramelli C, et al. (2001) [27], but are different from the result reported by Repka MX, et al. (2009) [19], Dickman A, et al. (2011) [24] and Yoon SW, et al. (2005) [25].

OCT has become a widely used tool in clinical ophthalmology. Normative data are provided automatically by OCT, but the database only includes individuals 18 years and older, limiting its use in children. There are several reports regarding the difference in the RNFL thickness between children and adults [28,29]. Possible explanations of difference from various studies include race, age, axial length, and disc area.

The differences between different versions of the device have also been found in adults, and may be due to the use of different algorithms between spectral and time domain OCT devices; making a comparison between different devices to be misleading [30,31].

Similarly, several studies on the variations of macular thickness measurements in normal subjects according to age and refractive error/axial length have been reported. Some studies have shown reductions in macular thickness with age, whereas others have found no significant correlation. More recent studies in which the third-generation Stratus OCT was used have shown average macular thickness and macular volume to be related to refractive error/axial length in normal subjects, as in histopathologic studies [32-35].

There are several limitations to our study, namely, the small number of patients. Since, the number of patients involved in the study is small as compared to those reported in most papers; so, a larger study I warranted to confirm our results.

Conclusion

Our results suggest that amblyopia seems to have a significant effect on the peripapillary RNFL thickness, in strabismic and anisometropic amblyopia.

Recommendation

- Increasing the sample size in future studies searching the same subject may give more accurate results.
- Including OCT examination of peripapillary RNFL in treatment and fellow up of amblyopic patient need further clinical base evidence that need further research.
- Further studies, including histopathological and instrumental studies with a greater number of patients, are required to confirm the differences between amblyopic and normal eyes.

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