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Original Research Article

A Hospital Based Prospective Comparative Assessment of the Retinal Nerve Fibre Layer Thickness in Different Types of Amblyopia

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Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to test the hypothesis that eyes with amblyopia may have thicker retina. Retinal nerve fiber layer thickness (RNFLT) was investigated in patients with different types of amblyopia.

Material & Methods: This prospective study was conducted on consecutive patients diagnosed with amblyopia seen at Department of Ophthalmology of a tertiary care centre in South Bihar, India for a duration of one & half years.

Results:. Thirty-eight eyes (38 patients) with anisometropic amblyopia, 25 eyes (25 patients) with strabismic amblyopia, 40 eyes (40 patients) with mixed amblyopia, and 10 eyes (10 patients) with anisometropia without amblyopia fulfilled the study criteria and were included in the study. Average RNFL thickness in anisometropic amblyopia and strabismic amblyopia was similar, and the difference was statistically insignificant compared with the fellow normal eyes ($P = 0.5$ and 0.6, respectively). All RNFL parameters in amblyopia groups were not statistically significantly different from the normal group. The difference between all the peripapillary parameters in strabismic amblyopia, anisometropic amblyopia, and mixed amblyopia compared with the normal group was not statistically significant. Differences between all the macular parameters with OCT in strabismic amblyopia, anisometropic amblyopia, and mixed amblyopia compared with the normal group were not statistically significant.

Conclusion: Our study showed that RNFL thickness was similar in amblyopic and non-amblyopic eyes between all three amblyopia groups.

Keywords: Anisometropic amblyopia, optical coherence tomography (OCT), Retinal nerve fiber thickness (RNFLT), strabismic amblyopia.

Introduction

Amblyopia is considered to be a developmental disorder of spatial vision that is associated with the presence of strabismus, anisometropia, or form deprivation early in life. [1] Amblyopia is defined as a unilateral or bilateral decrease of best-corrected visual acuity (BCVA) not attributable to structural or pathological ocular anomalies of the eyes and visual pathways.It occurs in 2% to 4% of the general population. [2] The amblyopic process may have an effect on various levels of the visual pathway. Shrinkage of cells in the lateral geniculate nucleus that receive input from the amblyopic eye [3,4] and a shift in the dominance pattern in the visual cortex. It is reduced best-corrected visual acuity in one or both eyes caused by abnormal visual experience during visual development. Causes include strabismus, image blur from refractive error, form deprivation, or a combination of these factors. A role for optic nerve abnormalities, termed “dysversion” or hypoplasia, in the genesis of visual loss diagnosed as amblyopia has been postulated by Lempert, who reported this optic nerve abnormality was present in optic nerve photographs in 45% of 205 amblyopic eyes. [5,6]

However, the effect of an amblyopic stimulus on the retinal ganglion cells is relatively less well-reported, and limited studies suggest variable results. Various authors found no difference in the thickness of the retinal nerve fiber layer (RNFL) between amblyopic and healthy eyes. [7] In contrast, Yen et al. and Yoon et al. reported a significant difference in RNFL thickness in eyes with anisometropic amblyopia compared with normal eyes [8,9] .With the introduction of imaging modalities like the scanning laser polarimetry and Optical coherence Tomography (OCT), it has become possible to objectively quantify the peripapillary RNFLT (retinal nerve fiber layer thickness) and macular thickness. 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. RNFL thickness correlates with disc area in children. [10,11] OCT has been used to compare the RNFL of amblyopic and fellow eyes of patients of varied ages. [12] The Stratus OCT-3 (Carl Zeiss Meditec, Dublin, USA)provides in vitro, high-resolution images of RNFL equivalent to 10 µm histological sections of the retina.

Hence, to test the hypothesis that eyes with amblyopia may have thicker retina, retinal nerve fiber layer thickness (RNFLT) was investigated in patients with different amblyopia.

Material & Methods

This prospective, interventional, comparative, longitudinal study was conducted on consecutive patients diagnosed with amblyopia seen at department of Ophthalmology of a tertiary care centre in South Bihar, India for a duration of one & half years. The institutional ethics committee approved the study protocol and the methods adhered to the tenets of the declaration of Helsinki for the use of human subjects in biomedical research

Inclusion criteria were:

- BCVA ≥20/20 in the better eye,
- Age between 5 years and 35 years,
- Intraocular pressure (IOP) <22 mmHg in both eyes,
- Clear ocular media,
- Normal fundus examination, and unilateral amblyopia due to strabismus, anisometropia, or both.
- Patients with anisometropic amblyopia, strabismic amblyopia, mixed amblyopia, and anisometropia without amblyopia.

Exclusion criteria:

- Subjects with recent intraocular surgery within 6 months
- Bilateral (emmetropic) amblyopia, deprivation amblyopia, coexisting nystagmus, and any other coexisting macular or retinal pathology that could affect final BCVA.
- Patients with pathologies that could affect the RNFL measurement (like cataract, retinal/macular pathology, glaucoma, abnormal discs/tilted discs, presence of systemic diseases, or neurological disorders producing RNFL damage), and in whom OCT images had a quality score <6
- Patients unwilling to participate in the study.

All patients underwent a complete ophthalmic examination, including BCVA testing(Log MAR chart), cover test, ocular motility evaluation, measurement of ocular deviation using the prism bar, slit lamp examination, applanation tonometry, optic disc, and RNFL examination with a 60D/78D/90D lens, fundus examination with indirect ophthalmoscopy, axial length measurement with A-scan, keratometry, peripapillary RNFL measurement with OCT Stratus 3.All tests to rule out strabismus were done. Intraocular pressure was measured using non contact tonometry wherever possible. Fundus examination was done using indirect ophthalmoscope and 20D condensing lens.Cycloplegic refraction using appropriate drug according to age was carried out in all children. Other visual function tests like color vision (Ishihara pseudo isochromatic plates), contrast sensitivity (Pelli–Robson contrast sensitivity chart), visual fields (Humphrey's field analysis/confrontation test/Amsler'schart), and electrophysiology tests were recorded wherever it was required and possible. Detailed ophthalmological examination both anterior and posterior segment was carried out in all children. OCT examinations were performed using a spectral domain optical coherence tomography (SD OCT)device (Carl Zeiss Meditec ,USA) by the same operator through dilated pupils of at least 5 mm in diameter. ''Fast RNFL map protocol'' consisting of three circular scans with diameters of 3.4 mm centered on the optic disc was performed along with the ''Macular Thickness Map'' protocol consisting of six radial scan lines centered on the fovea, each having a 6 mm transverse length. In order to obtain the best image quality, focusing and optimization settings were controlled and scans were accepted only if the signal strength (SS) was >6 (preferably 9–10). Scans with foveal decentration [i.e. with center point thickness standard deviation (SD) >10%] were repeated. MT was measured using calliper tool 350 µm nasally from the fovea between internal limiting membrane and retinal pigment epithelium. FT was measured at the center of fovea using calliper tool between internal limiting membrane and retinal pigment epithelium. In RNFLT measurement, total RNFL thickness was taken in the study. All findings were recorded for both the groups. Average of right eye (RE) and left eye (LE) values were taken for all the parameters in group 2. One month after first visit (post spectacle wear), amblyopic children (group 1) were asked to patch the normal fellow eye for 4 hours per day and perform near work such as reading, writing, drawing, mobile games, and activities like computer work. Parents were insisted upon maintaining a diary regarding the same to check for compliance. Group 1 children were followed up with BCVA, Macular Thickness (MT) ,Foveal Thickness (FT) , and RNFLT at 3, 6, 9, and12 months along with patch diary for children's compliance.

Statistical Methods:

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables. Initially, the outcome parameters were compared between amblyopic and normal subjects by using independent sample t-test. The mean values of all the outcome variables within amblyopic subjects were compared between the amblyopic and non-amblyopic eye at each follow-up interval separately using paired t-test. The change in the outcome parameters over the follow-up period within the amblyopic eye was compared by one-way repeated measure analysis of variance (ANOVA). Software IBM SPSS Statistics for Windows, Version 22.0. (IBM Corp Armonk, NY;2013) was used for statistical analysis.

Results

Table 1: Demographic features of patients in all study groups

	Anisometropic amblyopia Mean (SD), n=38				Strabismic amblyopia (SD), n=25		Mixed amblyopia (SD), n=40		Anisometropia without amblyopia (SD), n=10	
	HA	**N**	**MA**	**N**	**SA**	**N**	**Ma**	**N**	**AA**	**N**
Numbers	28	28	10	10	25	25	40	40	10	10
Age (years)	16.4 (7.3)		14.6 (6.4)		14.4 (6.2)		16.2 (7.3)		14.2 (7.2)	
Male: Female	22:6		5:5		17:8		32:8		3:7	
Refractive error (diopter, D)	4.86 (2.75)	1.72 (1.25)	−4.28 (3.5)	−1.38 (1.5)	1.78 (3.60)	1.65 (3.56)	1.05 (5.54)	0.75 (3.32)	−3.84 (2.90)	−1.96 (2.61)
Axial Length (mm)	22.28 (1.05)	22.48 (1.01)	24.86 (1.97)	23.77 (2.25)	23.27 (0.94)	23.17 (1.32)	23.87 (2.11)	23.67 (1.76)	24.06 (2.05)	23.17 (1.96)

[HA-Hypermetropia with amblyopia ; MA-Myopic amblyopia; Ma-mixed amblyopia ;
N-Contralateral normal eye; SD- Standard deviation; mm-millimeter]

Thirty-eight eyes (38 patients) with anisometropic amblyopia, 25 eyes (25 patients) with strabismic amblyopia, 40 eyes (40 patients) with mixed amblyopia, and 10 eyes (10 patients) with anisometropia without amblyopia fulfilled study criteria and were included for the study.

Table 2: Comparison of retinal nerve fiber layer thickness using Optical coherence tomography (Carl Zeiss Meditec,USA) parameters in different groups as compared with the normal fellow eye

Parameter	Anisometropic amblyopia (SD)	Normal (SD)	P	Mixed amblyopia (SD)	Normal (SD)	P	Strabismic amblyopia (SD)	normal (SD)	P	Anisometropia without amblyopia (SD)
Superior Avg	125.35 (22.36)	127.73 (17.63)	0.22	120.18 (26.74)	127 (18.06)	0.04	112.38 (23.27)	120.80 (28.38)	0.1	124.86 (22.01)
Inferior Avg	117.023 (24.02)	123.63 (22.72)	0.10	118.22 (24.22)	115.75 (20.37)	0.64	118.32 (29.19)	114.26 (21.3)	0.4	112.28 (20.03)
Temporal Avg	73.37 (27.36)	64.30 (12.84)	0.05	75.85 (25.4)	66.04 (13.79)	0.02	64.36 (16.23)	70.42 (18.8)	0.12	63.57 (15.21)
Nasal Avg	80.08 (31.62)	85.25 (21.10)	0.32	80.64 (25.75)	80.40 (23.79)	0.92	80.40 (26.53)	76.10 (23.43)	0.60	72.70 (25.49)
Avg Thickness	96.24 (16.27)	98.32 (12.8)	0.5	96.44 (15.12)	94.16 (19.91)	0.82	93.11 (14.95)	96.24 (17.56)	0.60	(14.55)

Average RNFL thickness in anisometropic amblyopia and strabismic amblyopia was similar, and the difference was statistically insignificant compared with the fellow normal eyes (P = 0.5 and 0.6, respectively). All RNFL parameters in amblyopia groups were not statistically significantly different from the normal group.

Table 3: Comparison of Macular parameters with Spectral Domain OCT in different Amblyopia groups to Normal

Parameter	Anisometropic amblyopia (SD)	Normal (SD)	P	Mixed amblyopia (SD)	Normal (SD)	P	Strabismic amblyopia (SD)	Normal (SD)	P	Anisometropia without amblyopia (SD)
Foveal Thickness	152.82 (26.78)	150.42 (23.84)	0.32	155.86 (32.99)	153.27 (27.65)	0.75	166.1 (36.85)	155.47 (29.94)	0.02	140.33 (22.26)
Total Macular vol	6.31 (0.55)	6.42 (0.38)	0.27	6.47 (0.49)	6.33 (0.5)	0.12	6.38 (0.43)	6.35 (0.42)	0.54	6.05 (0.42)
Outer Sup Avg Vol	1.18 (0.12)	1.23 (0.1)	0.05	1.21 (0.08)	1.19 (0.08)	0.05	1.19 (0.08)	1.19 (0.08)	0.7	1.14 (0.09)
Outer Inf Avg Vol	1.11 (0.13)	1.12 (0.07)	0.42	1.15 (0.1)	1.12 (0.11)	0.07	1.13 (0.09)	1.12 (0.09)	0.55	1.08 (0.08)
Outer Temporal Avg vol	1.1 (0.08)	1.1 (0.06)	0.50	1.12 (0.09)	1.09 (0.1)	0.10	1.09 (0.08)	1.09 (0.09)	0.52	1.02 (0.1)
Outer Nasal Avg Vol	1.27 (0.12)	1.28 (0.08)	0.50	1.29 (0.14)	1.28 (0.13)	0.68	1.28 (0.11)	1.27 (0.09)	0.36	1.21 (0.08)
Inner Sup Avg Vol	0.38 (0.04)	0.39 (0.03)	0.2	0.39 (0.03)	0.38 (0.03)	0.52	0.38 (0.03)	0.38 (0.03)	0.80	0.37 (0.02)
Inner Inf Avg Vol	0.38 (0.04)	0.39 (0.03)	0.20	0.4 (0.03)	0.39 (0.03)	0.10	0.40 (0.03)	0.39 (0.03)	0.80	0.37 (0.03)
Inner Temporal Avg vol	0.36 (0.04)	0.37 (0.03)	0.2	0.37 (0.03)	0.37 (0.03)	0.82	0.37 (0.03)	0.37 (0.03)	0.52	0.35 (0.02)
Inner Nasal Avg Vol	0.38 (0.05)	0.39 (0.03)	0.40	0.39 (0.04)	0.39 (0.03)	0.60	0.38 (0.03)	0.39 (0.03)	0.7	0.37 (0.02)
Central Foveal Vol	0.14 (0.02)	0.14 (0.02)	1	0.14 (0.02)	0.14 (0.03)	0.64	0.15 (0.02)	0.14 (0.02)	0.06	0.13 (0.02)

Differences between all the macular parameters with OCT in strabismic amblyopia, anisometropic amblyopia, and mixed amblyopia compared with the normal group were not statistically significant.

Discussion

Amblyopia is reduced best-corrected visual acuity in one or both eyes caused by abnormal visual experience during visual development. Causes include strabismus, image blur from refractive error, form deprivation, or a combination of these factors. While most of the deficit is felt due to impairment of cortical development, changes have been seen in the lateral geniculate nucleus of non-human primates and humans following visual deprivation amblyopia during the neonatal period. [13,14] A role for optic nerve abnormalities, termed “dysversion” or hypoplasia, in the genesis of visual loss diagnosed as amblyopia has been postulated by Lempert, who reported this optic nerve abnormality was present in optic nerve photographs in 45% of 205 amblyopic eyes. [15,16] More recently Lempert has reported reduced optic disc rim areas or both amblyopic and fellow eyes with the reduction most prominent in the amblyopic eyes. [17] 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. RNFL thickness correlates with disc area in children. [18] OCT has been used to compare the RNFL of amblyopic and fellow eyes of patients of varied ages. [19,20] One study found a small statistically significant difference between eyes for anisometropic amblyopia (amblyopic eyes thicker) and no difference for strabismic amblyopia.19 Another study found no difference but had insufficient numbers to evaluate subgroups by cause. [20]

Thirty-eight eyes (38 patients) with anisometropic amblyopia, 25 eyes (25 patients) with strabismic amblyopia, 40 eyes (40 patients) with mixed amblyopia, and 10 eyes (10 patients) with anisometropia without amblyopia fulfilled study criteria and were included for the study. Average RNFL thickness in anisometropic amblyopia and strabismic amblyopia was similar, and the difference was statistically insignificant compared with the fellow normal eyes (P = 0.5 and 0.6, respectively). All RNFL parameters in amblyopia groups were not statistically significantly different from the normal group. The difference between all the peripapillary parameters in strabismic amblyopia, anisometropic amblyopia, and mixed amblyopia compared with the normal group was not statistically significant. Differences between all the macular parameters with OCT in strabismic amblyopia, anisometropic amblyopia, and mixed amblyopia compared with the normal group were not statistically significant

Using SD-OCT, Chen et al [21] compared the macular and RNFL thickness in children with anisometropic amblyopia. They reported that the average thickness of the outer macular ring and RNFL were significantly thicker in eyes with anisometropic amblyopia than those with emmetropia. However, following adjustment for axial length and refractive error, this difference was not significant. Furthermore, the macular parameters were not different between treated and untreated amblyopic eyes in their group. They concluded that macular and RNFL thicknesses appear to be more extensively associated with differences in axial length and refraction than with amblyopic development. Kasem et al [22] investigated the changes in macular parameters (thickness, volume) and peripapillary retinal nerve fiber layer (RNFL) thickness (RNFLT) in different cases of amblyopia versus the healthy fellow eyes using OCT. There were significant differences in mean Central Macular Thickness (CMT), mean average macular thickness, mean macular volume, and the mean global RNFLT in the amblyopic eyes versus the fellow eyes. Age and axial length were the only independent variables that statistically significantly correlated with the CMT. They concluded that unilateral amblyopic eyes were prone to have a higher CMT and thicker global RNFL than those of the healthy fellow eyes. However, we could not find any significant difference in the amblyopia group.

Conclusion

MT and FT which were more in amblyopic eyes as compared to normal fellow eyes and normal eyes of normal children, decreased with improvement in BCVA after occlusion therapy. However, there was no difference in RNFLT between amblyopic eyes and normal fellow eyes and normal eyes of normal children before and after occlusion therapy. The several levels of the visual pathways and posterior segment of the eye might be or not be affected in different types of amblyopia.

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