Original Article

Analysis of macular, foveal, and retinal nerve fiber layer thickness in children with unilateral anisometropic amblyopia and their changes following occlusion therapy

V Kavitha, Mallikarjun M Heralgi[1], Patel Deep Harishkumar[2], Sneha Harogoppa[3], H M Shivaswamy[4], H Geetha[5]

Purpose: To analyze macular thickness (MT), foveal thickness (FT), and retinal nerve fibre layer thickness (RNFLT) in children with unilateral anisometropic amblyopia and their changes following occlusion therapy. **Methods:** A prospective, longitudinal, and comparative study of 60 children aged between 5 and 18 years consisted of two groups, group 1: 30 children with unilateral anisometropic amblyopia; group 2: 30 normal children. Best corrected visual acuity (BCVA), a detailed ocular examination, spectral domain optical coherence tomography for MT, FT, and RNFLT in both eyes were done at visit one (baseline) and every 3 months for a year following occlusion therapy (initiated one month after first visit) in group 1. **Results:** Mean BCVA, MT, FT, and RNFLT in amblyopic eyes at first visit were 0.63 ± 0.405, 286.9 ± 6.522 µm, 195.90 ± 8.462 µm, and 100.87 ± 6.240 µm, respectively and at last visit after occlusion therapy were 0.50 ± 0.318, 248.9 ± 11.681 µm, 169.47 ± 10.941 µm, and 99.43 ± 5.722 µm, respectively. At first visit, mean BCVA, MT, FT, and RNFLT in nonamblyopic eyes (group 1) were 0 ± 0, 240 ± 10.447 µm, 159.27 ± 9.285 µm, 98.63 ± 4.723 µm and in normal eyes (group 2: average of right and left eyes) were 0 ± 0, 239.8 ± 4.294 µm, 143.6 ± 4.61 µm, 100.5 ± 2.895 µm, respectively. **Conclusion:** MT and FT, which were more in amblyopic eyes as compared to normal fellow eyes and group 2, decreased with improvement in BCVA after occlusion therapy. However, there was no difference in RNFLT between amblyopic eyes and normal fellow eyes and group 2 before and after occlusion therapy.

Access this article online

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_1438_18

Quick Response Code:

Key words: Amblyopia, foveal thickness, macular thickness, occlusion therapy, RNFL thickness, SD OCT

Amblyopia is defined as decrease of visual acuity in one eye when caused by abnormal binocular interaction or occurring in one or both eyes as a result of pattern vision deprivation during visual immaturity, for which no cause can be detected during the physical examination of the eye (s) and which in appropriate cases is reversible by therapeutic measures.[1] With advent of optical coherence tomography (OCT), etiopathology of amblyopia is being better understood as it is one of the best tools to study the structural changes in retina.[2] Occlusion therapy has long been the mainstay of amblyopia treatment.[1] Various studies are available documenting changes in macular thickness (MT), foveal thickness (FT), and retinal nerve fibre layer thickness (RNFLT) in amblyopic eyes.[3-8] However, there are only few studies available on analysis of these parameters following occlusion therapy. Hence, the purpose of our study was not only to analyze the structural changes in retina (MT, FT, and RNFLT) in unilateral anisometropic amblyopic eyes and compare the same with the normal fellow eyes and normal eyes of normal children but also to understand the same following occlusion therapy.

Methods

This prospective, interventional, comparative, longitudinal study was carried out at a tertiary care eye hospital in South India between October 2015 and June 2017. The study was approved by the institutional review board and adhered to all the principles mentioned in the Declaration of Helsinki 2000. Based on previous literature on outcome variable of visual acuity in LogMAR scale for 90% statistical power, 5% level of type 1 error, 10% type 2 error, and 95% confidence interval (CI) or at 5% level of significance, the estimated sample size was 60 children, 30 in each group. They were divided equally into two groups. Group 1 included children with unilateral anisometropic amblyopic eyes and normal fellow eyes (nonamblyopic eyes); group 2 included normal eyes of normal children. Inclusion Criteria: 1) Children of either sex aged between 5 and 18 years with unilateral anisometropic amblyopia (difference in best corrected visual acuity (BCVA) of ≥0.2 LogMAR between two eyes) were included in group 1. 2) Uncorrected visual acuity (UCVA) of LogMAR 0.00 in

Consultant, Department of Pediatric Ophthalmology, Sankara Eye Hospital, [1]Consultant, Department of Cornea and Refractive Services Sankara Eye Hospital, [2]Registrar, Sankara Eye Hospital, [3]Fellow in Paediatric Ophthalmology, Sankara Eye Hospital, [4]Optometrist, Sankara Eye Hospital, [5]School Screening Project Coordinator, Sankara Eye Hospital, Harakere, Shimoga, Karnataka, India

Correspondence to: Dr. V Kavitha, Consultant, Department of Pediatric Ophthalmology, Sankara Eye Hospital, Harakere, Shimoga - 577 202, Karnataka, India. E-mail: kavithachalam2@gmail.com

Manuscript received: 26.08.18; Revision accepted: 12.03.19

Cite this article as: Kavitha V, Heralgi MM, Harishkumar PD, Harogoppa S, Shivaswamy HM, Geetha H. Analysis of macular, foveal, and retinal nerve fiber layer thickness in children with unilateral anisometropic amblyopia and their changes following occlusion therapy. Indian J Ophthalmol 2019;67:1016-22.

both eyes was included in group 2. 3) Children with normal neurological, ocular, and systemic examination. 4) Those willing for follow-up. Exclusion criteria: 1) Previous history of spectacle wear/occlusion therapy/ocular surgery. 2) Refractive error correction greater than 6 diopter spherical power and 3 diopter cylindrical power. 3) Presence of strabismus/nystagmus/hearing impairment/developmental delay. 4) Not compliant for spectacle wear and/or occlusion therapy. 5) Children who had poor fixation cooperation for SD OCT test, due to poor vision or lower age. 6) Children who have come for less than three follow-ups. After satisfying the inclusion and exclusion criteria, written informed consent from every child's parent or parents was taken after counseling them regarding the nature of the study. In group 2, first two normal children attending the outpatient department every day were recruited in the study. Detailed history regarding any ocular and systemic conditions was noted. UCVA and BCVA for distance using LogMAR three meter chart (English letters or symbols chart) and near vision using Snellen chart were recorded by a single person. All tests to rule out strabismus were done. Intraocular pressure was measured using noncontact 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's chart), 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 (Topcon 3D Maestro 2000 series, Tokyo, Japan) 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 caliper 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 (postspectacle wear), amblyopic children (group 1) were asked to patch the normal fellow eye for 4 hours per day and perform near activities such as reading, writing, drawing, mobile games, and computer work. Parents were insisted upon maintaining a diary regarding the same to check for compliance. Group 1 children were followed up with BCVA, MT, FT, and RNFLT at 3, 6, 9, and 12 months along with patch diary for children's compliance. Data were analyzed using SPSS software (Statistical Package for Social Science) and by using the paired Student '*t*' test.

Statistical methods: MT, FT, and RNFLT were considered as outcome variables. Amblyopia was considered as explanatory variable. 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 nonamblyopic 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

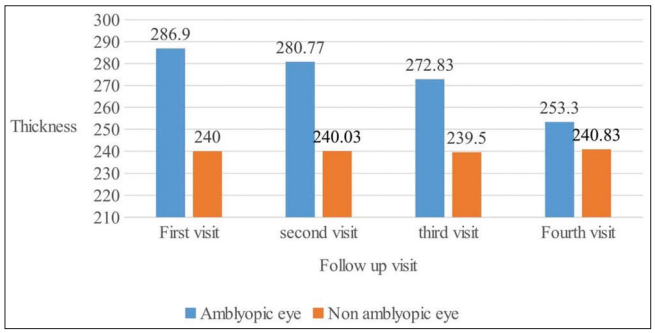
A total of 60 children aged between 5 and 18 years were included in the analysis. Out of which 30 children had unilateral amblyopia (Group 1) and 30 children were normal (group 2). The mean age in group 1 and 2 were 9.77 ± 2.674 and 9.70 ± 2.20 years, respectively ($P = 0.916$). In group 1, 56.66% (17) and 43.33% (13) were male and female children, respectively. Likewise in group 2, 60% (18) and 40% (12) were male and female children, respectively. In group 1, 12 (40%) had right eye (RE) amblyopia and 18 (60%) had left eye (LE) amblyopia. In group 1, 7 (23.3%) children had myopia, 5 (16.7%) had hypermetropia and 18 (60%) had astigmatism. The baseline values of mean LogMAR BCVA, MT, FT, and RNFLT in group 1 amblyopic eyes were 0.63 ± 0.405, 286.9 ± 6.522 μm, 195.9 ± 8.462 μm, and 100.8 ± 6.240 μm and nonamblyopic eyes were 0.00 ± 0.00, 240 ± 10.447 μm, 159.27 ± 9.285 μm, and 98.63 ± 4.723 μm, respectively; in group 2 (average of RE and LE in normal patients), they were 0.00 ± 0.00, 239.8 ± 4.294 μm, 143.6 ± 4.610 μm, and 100.5 ± 2.895 μm, respectively.

At first visit, the difference in mean BCVA, MT, and FT between amblyopic eyes (0.63 ± 0.405, 286.9 ± 6.522 μm, and 195.90 ± 8.462 μm) and normal eyes of normal group (0.00 ± 0.00, 239.8 ± 4.294 μm, and 143.6 ± 4.610 μm) was statistically significant (P value < 0.001). Similarly, the difference between amblyopic eyes and nonamblyopic eyes (0.00 ± 0.00, 240 ± 10.447 μm, and 159.27 ± 9.285μm) was statistically significant (P value < 0.001). However, the difference in mean RNFLT between amblyopic eyes (100.87 ± 6.24μm) and normal eyes (100.5 ± 2.895 μm); and nonamblyopic eyes (98.63 ± 4.723 μm) was statistically not significant (P value: 0.802 and 0.131, respectively). The mean LogMAR BCVA in amblyopic eyes in visit 1 (baseline) and following occlusion therapy at 3, 6, 9, and 12 months were 0.63 ± 0.405, 0.56 ± 0.368, 0.51 ± 0.374, 0.46 ± 0.330, and 0.50 ± 0.318, respectively. An improvement in BCVA following occlusion therapy was seen in all patients. Table 1 shows comparison of BCVA, MT, FT, and RNFLT between amblyopic eyes, nonamblyopic eyes, and normal eyes at various follow-ups. Graph 1 shows comparison of MT between amblyopic and nonamblyopic eyes at various follow-ups. Graph 2 shows comparison of FT between amblyopic and nonamblyopic eyes at various follow-ups. Fig. 1 shows OCT picture of macula of amblyopic eye at first visit and Fig. 2 shows OCT picture of macula of amblyopic eye at last visit following occlusion therapy.

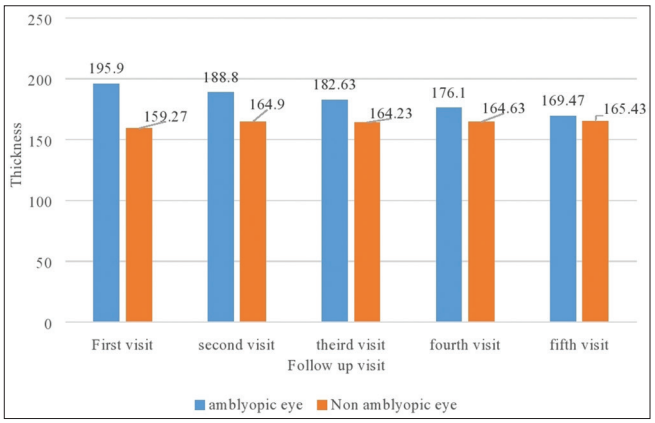
Table 1: Comparison of mean BCVA, MT, FT, and RNFLT between amblyopic eyes, nonamblyopic eyes, and normal eyes at various follow-ups

	Group 1- Amblyopic eyes			
	BCVA	MT (μm)	FT (μm)	RNFLT (μm)
	P<0.001	(mean±STD)	(mean±STD)	(mean±STD)
1st visit (0 M)	0.63±0.405	286.9±6.022	195.90±8.462	100.87±6.241
2nd visit (3 M)	0.56±0.368	280.77±7.677	188.800±8.903	99.30±4.843
3rd visit (6 M)	0.51±0.374	272.83±9.476	182.633±7.924	99.03±5.555
4th visit (9 M)	0.46±0.330	253.30±11.065	176.10±11.309	101.23±5.276
5th visit (12 M)	0.50±0.318	248.90±11.681	169.467±10.941	99.43±5.722
		Group 1-Normal fellow eyes		
1st visit (0 M)	0.00±0.00	240±5.977	159.27±9.285	98.63±4.723
	P<0.001	*P*<0.001	*P*<0.001	*P* 0.131
2nd visit (3 M)	0.00±0.00	240.03±5.678	164.90±7.840	100.60±6.295
	P<0.001	*P*<0.001	*P*<0.001	*P* 0.368
3rd visit (6 M)	0.00±0.00	239.50±5.335	164.23±8.157	99.03±4.642
	P<0.001	*P*<0.001	*P*<0.001	*P* 1.000
4th visit (9 M)	0.00±0.00	240.83±5.977	164.63±7.981	99.03±5.314
	P<0.001	*P*<0.001	*P*<0.001	*P* 0.089
5th visit (12 M)	0.00±0.00	239.47±5.569	165.43±7.771	99.60±5.500
	P<0.001	*P*<0.001	*P* 0.098	*P* 0.917
		Group 2- Normal eyes of normal children (average of RE and LE values)		
1st visit (0 M)	0.00±0.00	239.8±4.294	143.6±4.610	100.5±2.895
	P<0.001	*P*<0.001	*P*<0.001	*P* -0.802

BCVA: Best corrected visual acuity, MT: Macular thickness, FT: Foveal thickness, RNFLT: retinal nerve fiber thickness, M: month, RE: Right eye, LE: Left eye



Graph 1: Comparison of macular thickness between amblyopic and nonamblyopic eyes at various follow-ups



Graph 2: Comparison of foveal thickness between amblyopic and nonamblyopic eyes at various follow-ups

Correlation between improvement in BCVA and decrease in MT and FT: There is a weak negative correlation between change in MT amblyopic eye and change in BCVA amblyopic eye (*r* value: −0.026, *P* value: 0.891). There is also a weak negative correlation between change in FT amblyopic eye and change in BCVA amblyopic eye (*r* value: −0.020, *P* value: 0.917).

The subgroup analysis based on age group is represented with the mean differences, 95% CI and *P* values in Table 2. We have performed univariate and multivariate logistic regression analysis to identify factors independently associated with change in BCVA, change in FT and MT. We have considered age, gender, and baseline values of BCVA, MT, and FT as explanatory parameters. The findings are presented in Table 3. In the three groups of refractive error, myopia, hypermetropia, and astigmatism respectively, the mean change in BCVA was 0.24 ± 0.13, 0.36 ± 0.11, and 0.34 ± 0.22 (*P* value: 0.295); mean change in MT was 44.57 ± 9.5, 34.4 ± 6.5, and 36.5 ± 15.1 (*P* value: 0.194); mean change in FT was 25.86 ± 6.89, 28.6 ± 8.65, and 26.06 ± 9.19 (*P* value: 0.593); mean change in RNFLT was 3.57 ± 4.43, −0.6 ± 9.69, and 1.17 ± 7.3 (*P* value: 0.331).

Discussion

Amblyopia had been thought to be a disease associated with an abnormality of the retina.[9] However, amblyopia-induced cerebral changes were later shown to mainly occur in the visual cortex and the lateral geniculate body. In an experimental study, Von Noorden *et al*. have suggested that the mechanism

Table 2: Subage group comparison of mean of different parameters between first and fifth visit in group 1

Time periods	Affected Eye Mean±SD	Mean difference	95% CI		*P*
			lower	Upper	
Age group: 5-10 years (Amblyopic eyes, *n*=20)					
I. BCVA					
1st visit (Base line)	0.70±0.46				
5th visit	0.53±0.34	0.27	0.145	0.405	<0.001
II. MT					
1st visit (Base line)	288.20±6.62				
5th visit	251.40±12.51	36.800	30.099	43.501	<0.001
III.FT					
1st visit (Base line)	197.55±7.66				
5th visit	169.75±11.80	27.800	23.662	31.938	0.004
IV. RNFLT					
1st visit (Base line)	100.40±5.67				
5th visit	99.20±6.30	1.20	23.187	30.113	0.457
Age group: 11-15 years (Amblyopic eyes, *n*=10)					
I. BCVA					
1st visit (Base line)	0.51±0.25				
5th visit	0.38±0.21	0.37	0.174	0.575	0.009
II. MT					
1st visit (Base line)	284.40±5.82				
5th visit	243.90±8.23	40.50	32.935	48.065	<0.001
III.FT					
1st visit (Base line)	192.60±9.42				
5th visit	99.90±4.61	1.900	-3.437	7.237	0.441
IV. RNFLT					
1st visit (Base line)	101.80±7.50				
5th visit	99.90±4.61	1.900	-3.437	7.237	0.441

BCVA: Best corrected visual acuity, F: foveal thickness, MT: macular thickness, RNFLT: retinal nerve fiber thickness

responsible for amblyopia may be inadequate visual stimulation of the fovea during early childhood, abnormal binocular interaction or incompatibility in the visual information received by the two eyes, or a mixture of these problems.[10] Yen *et al.* hypothesized that the normal postnatal reduction (apoptosis) of retinal ganglion cells is arrested in amblyopia and predicted that this would cause increased RNFLT. If this does indeed occur, it is likely that the arrest of normal postnatal changes would result not only in increased RNFLT but also would affect the normal maturation of the macula, including movement of Henle's fibers away from the foveola and a decrease in foveal cone diameter. This would explain increased foveal thickness in cases of amblyopia. Furthermore, because of the reduced apoptosis of retinal ganglion cells, the thickness of the ganglion cell layer in the macula would also be increased.[11] Absence of normal vision stimulation may also lead to less or no apoptosis of retinal ganglion cells in amblyopic eyes, eventually leading to thicker RNFL of the amblyopic eye than nonamblyopic eye.[12,13]

Few studies have suggested that there is no difference in macular or RNFL thicknesses in children with unilateral amblyopia.[14-17] On the contrary, few studies, however, have shown that thickening of the RNFL occurs in anisometropic and strabismic amblyopia.[11,12] Huynh *et al.* and Pang *et al.* showed a thicker fovea in unilateral amblyopia,[18,19] while Al-Haddad *et al.* found a thicker macula in anisometropic amblyopia.[6] Other studies, however, have shown thickening of RNFL, macula, and fovea in children with amblyopia.[3,5,6,11,18] The results of various studies is shown in Table 4. OCT is a rapid, noninvasive, office-based imaging technique allowing objective quantification of retinal structures with high resolution, including determination of peripapillary RNFL thickness and macular thickness.

In our study, of 60 children with anisometropic amblyopia, the MT was more in amblyopic eyes (286.9 ± 6.52 μm) compared to nonamblyopic fellow eyes (240 ± 10.45 μm) and normal eyes of normal children (239.8 ± 4.294 μm). This difference which was statistically significant and was similar to other studies.[4,11,13,17] In our study, FT was significantly more ($P < 0.001$) in amblyopic eyes (195.9 ± 8.462 μm) compared to normal fellow eyes (159.27 ± 9.285 μm) and normal eyes of normal children (143.6 ± 4.610 μm). This difference was statistically significant. Similar results were found in other studies.[6,13,20] With respect to RNFLT, we found no statistically significant difference in amblyopic eyes compared to normal fellow eyes and normal eyes of normal children. This was consistent with other studies.[14-17] Table 2 shows the MT, FT, and RNFLT among various studies. Furthermore, on analyzing the effectiveness of occlusion therapy on BCVA, MT, FT, and RNFLT at 3, 6, 9, and 12 months, we found an improvement in BCVA in all patients following occlusion therapy at the end of

Table 3: Univariate and multivariate linear regression analysis

Parameter	Unadjusted regression coefficient	95%CI		*P*
		Lower	Upper	
Univariate linear regression analysis of factors influencing change in BCVA in the amblyopic eyes				
Age	-0.070	-0.032	0.022	0.712
Gender (Base line=female)	-0.200	-0.214	0.66	0.066
BCVA	0.504	0.078	0.385	0.004
FT	0.161	-0.005	0.012	0.395
MT	0.216	-0.005	0.017	0.252
Univariate linear regression analysis of factors influencing change MT in the amblyopic eyes				
Age	0.262	-0.549	44.037	0.009
Gender (Base line=female)	-0.316	-17.650	1.514	0.096
BCVA	-0.585	-29.082	-8.785	0.001
FT	0.044	-0.532	0.668	0.670
MT	0.457	0.227	1.612	0.011
Univariate linear regression analysis of factors influencing change FT in the amblyopic eyes				
Age	-357	-2.260	0.013	0.053
Gender (Base line=female)	-0.192	-9.544	3.128	0.309
BCVA	0.004	-7.943	8.097	0.985
FT	0.159	-0.222	0.537	0.402
MT	-0.034	-0.542	0.455	0.858
Multivariate linear regression analysis of factors influencing change MT in the amblyopic eyes				
	Adjusted Regression coefficient			
BCVA	-0.676	-29.460	-14.244	<0.001
MT	4.930	0.664	1.610	<0.001

BCVA: Best corrected visual acuity, FT: foveal thickness, MT: macular thickness

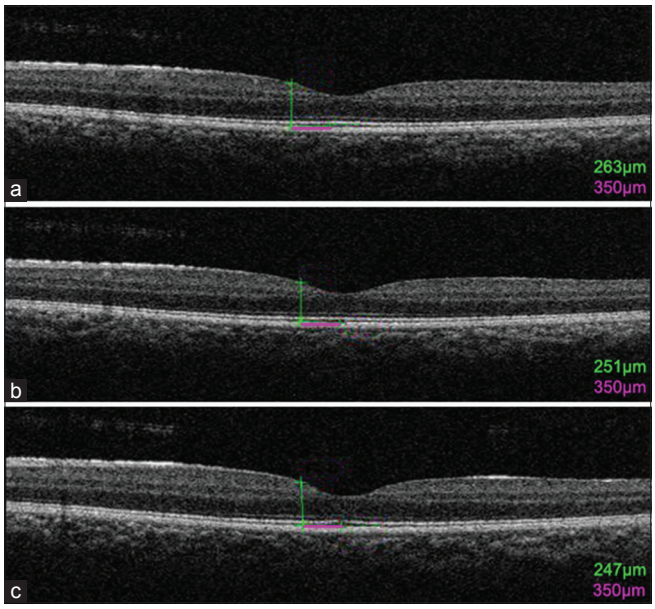


Figure 1: OCT image of macular thickness of amblyopic eye: (a) at first visit- baseline, following occlusion therapy (b) at 6 months and (c) at 12 months

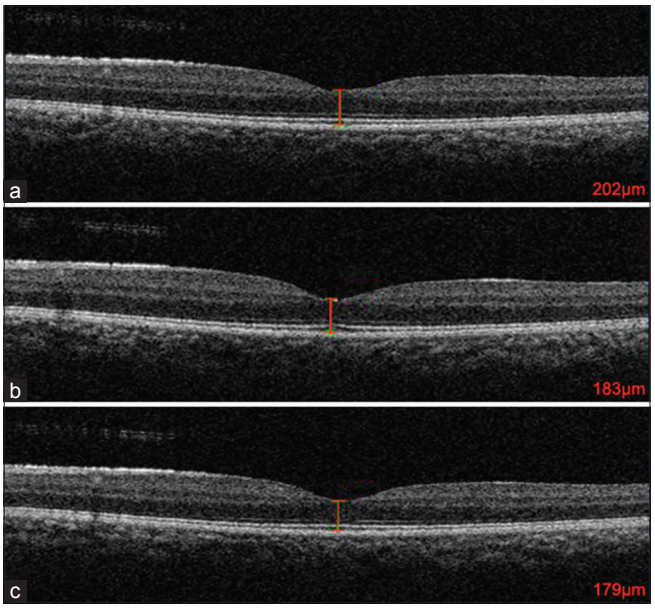


Figure 2: OCT picture of foveal thickness of amblyopic eye: (a) at first visit- baseline, following occlusion therapy (b) at 6 months and (c) at 12 months

1 year, minimum improvement being two letters seen in two children and maximum being five lines seen in five children. We found statistically significant reduction in MT and FT on each visit compared to baseline [visit 1], but there was no statistically significant difference in RNFLT, post occlusion therapy in amblyopic eyes. Tugcu *et al.* studied macular thickness in the persistent amblyopic and resolved amblyopic eyes and did not find significant difference between the two groups.[21] Chen *et al.* compared the macular thickness of the amblyopic eyes with those of fully corrected previous amblyopic

Table 4: MT, FT, and RNFLT in amblyopic eyes among various studies

Studies (author, year)	Study size (*n*)	Age (years)	Type of amblyopia	OCT type	RNFLT	MT	FT
Yen *et al*.[11] (2004)	38	26.4±18.3	M	TDOCT (2)	increased	not studied	
	18	25.4±18.6	A		increased	not studied	
	20	27.4±18.6	S		no difference	not studied	
Yoonet al.[5]	31	7.7 (5-12)	HA	TD-OCT (3)	increased	not studied	
Kee *et al*.[15] (2006)	26	8 (4-12)	M	TD-OCT (3)	no difference	no difference	
	6	4 to 12	S		no difference	no difference	no difference
Hunyh *et al*.[18] (2009)	48	6 and 12	M	TD-OCT (3)	no difference	increase FMT	
Pang *et al*.[3] (2011)	31	9.6 (5-18)	M	TD-OCT (3)	not studied	no difference	
AL-Haddad *et al*.[6] (2011)	45	20±12	M	SD-OCT	no difference	no difference	
Alotaibi *et al*.[7] (2011)	93	8.7 (5-12)	M	OCT	increased	no difference	
	36		S		increased	no difference	
	33		A		increased	increase MT and FV	
	24		AS		increased	no difference	
Rajvi Z[17] (2014)	93	7±2	A	SD-OCT	not studied	no difference	increased in moderate to severe amblyopia
Atakan *et al*.[8] (2015)	30	6 to 25	S	SD-OCT	no difference	no difference	no difference
	31	7 to 15	A		no difference	no difference	no difference
Yoon and Chun[20] (2017)	22	3 to 9	A	OCT	not studied	no difference	no difference
Kasem and Badawi[23] (2017)	64	7 to 32	A	OCT	increased	increased	

MT: macular thickness, FT: foveal thickness, FV: foveal volume, RNFLT: retinal nerve fibre layer thickness, M: Mixed amblyopia, A: anisometropic amblyopia, HA: Hyperopic amblyopia S: strabismic amblyopia, SD-OCT: spectral domain OCT, TD-OCT: time domain OCT

eyes and nonamblyopic controls and found there was no significant difference among the three groups.[22] In contrast, Pang *et al*. reported that the central macular thickness in myopic anisometropic amblyopia significantly reduced after amblyopia treatment.[19] However, the measurements in their study were not adjusted for axial length and refractive error. Analysis on correlation between BCVA and MT and FT showed a weak negative correlation which implies that with improvement of BCVA in amblyopic eyes following occlusion therapy there was normalization (or reduction) of MT and FT as revealed in OCT.

In group 1, on subage group analysis and comparison between 5 and 10 years (20 children) and 11–15 years (10 children), we observed a definite change (difference between first and last visit) in BCVA (0.17/0.13), MT (36.80/40.60), and FT (27.80/23.80) following occlusion therapy but there was no much change in RNFLT in both the groups (1.20/1.10). The change was greater in BCVA improvement and reduction of FT in 5–10 years age group, whereas the change was greater in reduction of MT in 11–15 years. The difference in RNFLT between the two groups was minimal. However, differences between both the subage groups are not statistically significant. There is no specific reason that we could attribute to this difference and trend in findings among the two age groups. However, larger and equal sample size is required to understand.

Following occlusion therapy, the mean BCVA change was greatest in the hypermetropic group (five children) which is revealed by the maximum change in FT, although least change was seen on MT. However with least change in BCVA in the myopic group (seven children), maximum change was noted on MT. This observation made may not be significant because the number of children in each subage group and each refractive error group is not the same, our criteria were only to include children with unilateral anisometropic amblyopia. To analyze in detail, we need larger and same numbers in each subgroup (based on both age wise and type of refractive error) and with longer follow-up period.

On univariate and multivariate linear regression analysis, none of the baseline parameters had shown any statistically significant association with change in BCVA and FT in the affected eye; however, univariate linear regression analysis showed baseline BCVA and baseline MT values to have statistically significant association with change in MT. Multivariate linear regression analysis showed base line BCVA to be negatively associated with change in MT (P value < 0.001) and baseline MT to be positively associated with change in MT (P value < 0.001).

Limitations: It is difficult to establish the independent association between various factors like age, gender, and type of refractive error and severity of refractive error. Subgroup analysis may not give any meaningful conclusions due to small sample size. Hence, we consider this as limitation of the study. Bilateral refractive, strabismic, and visual deprivation amblyopia were not included in the study. Choroidal thickness and different layers of retina were not analyzed. Sustainability

of the improved BCVA and changes in anatomical layers of retina following discontinuation of occlusion therapy could not be assessed.

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. Therefore, we can hypothesize that occlusion therapy can help in restoring the process of postnatal reduction of ganglion cells as evidenced by reduction in MT and FT on OCT. We suggest that further larger studies addressing the limitations of the current study are needed to validate the results of the current study.

Acknowledgements

We acknowledge all the patients and their parents who were involved in the study, colleagues and our family members for their immense help.

We also acknowledge statistician, Dr. G. MuraliMohan Reddy.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Von Noorden GK, Campos EC. Binocular Vision and Ocular Motility: Theory and Management of Strabismus. 6th ed. St. Louis: Mosby; 2002.
2. Liu H, Zhong L, Zhou X, Jin QZ. Macular abnormality observed by OCT in children with amblyopia failing to achieve normal visual acuity after long-term treatment. J Pediatr Ophthalmol Strabismus 2010;47:17-23.
3. Pang Y, Goodfellow GW, Allison C, Block S, Frantz KA. A prospective study of macular thickness in amblyopic children with unilateral high myopia. Invest Ophthalmol Vis Sci 2011;52:2444-9.
4. Agrawal S, Singh V, Singhal V. Cross-sectional study of macular thickness variations in unilateral amblyopia. J Clin Ophthalmol Res 2014;2:15-7.
5. Yoon SW, Park WH, Baek SH, Kong SM. Thicknesses of macular retinal layer and peripapillary retinal nerve fiber layer in patients with hyperopic anisometropic amblyopia. Korean J Ophthalmol 2005;19:62-7.
6. Al-Haddad CE, Mollayess GM, Cherfan CG, Jaafar DF, Bashshur ZF. Retinal nerve fibre layer and macular thickness in amblyopia as measured by spectral-domain optical coherence tomography. Br J Ophthalmol 2011;95:1696-9.
7. Alotaibi AG, Al Enazi B. Unilateral amblyopia: Optical coherence tomography findings. Saudi J Ophthalmol 2011;25:405-9.
8. Atakan M, Culfa S, Calli U, Penbe AD, Atakan TG. Evaluation of retinal nerve fibre layer and macular thickness in amblyopia. J Clin Exp Ophthalmol 2015;6:437.
9. McNeil NL. Patterns on visual defects in children. Br J Ophthalmol 1955;39:688-701.
10. Von Noorden GK, Dowling JE, Ferguson DC. Experimental amblyopia in monkeys. I. Behavioral studies of stimulus deprivation amblyopia. Arch Ophthalmol 1970;84:206-14.
11. Yen MY, Cheng CY, Wang AG. Retinal nerve fiber layer thickness in unilateral amblyopia. Invest. Ophthalmol Vis Sci 2004;45:2224-30.
12. Lewis TL, Maurer D. Multiple sensitive periods in human visual development: Evidence from visually deprived children. Dev Psychobial 2005;46:163-83.
13. Wu SQ, Zhu L, Xu QB, Xu JL, Zhang Y. Macular and peripapillary retinal nerve fiber layer thickness in children with hyperopic anisometropic amblyopia. Int J Ophthalmol 2013;6:85-9.
14. Altintas O, Yuksel N, Ozkan B, Caglar Y. Thickness of the retinal nerve fiber layer, macular thickness, and macular volume in patients with strabismic amblyopia. J Pediatr Ophthalmol Strabismus 2005;42:216-21.
15. Kee SY, Lee SY, Lee YC. Thicknesses of the fovea and retinal nerve fiber layer in amblyopic and normal eyes in children. Korean J Ophthalmol 2006;20:177-81.
16. Baddini-Caramelli C, Hatanaka M, Polati M. Thickness of the retinal nerve fiber layer in amblyopic and normal eyes: A scannig laser polarimetry study. J AAPOS 2001;5:82-4.
17. Rajavi Z, Moghadasifar H, Feizi M, Haftabadi N, Hadavand MR, Yaseri M, *et al.* Macular thickness and amblyopia. J Ophthalmic Vis Res 2014;9:478-83.
18. Huynh SC, Samarawickrama C, Wang XY, Rochtchina E, Wong TY, Gole GA, *et al.* Macular and nerve fiber layer thickness in amblyopia: The Sydney childhood eye study. Ophthalmology 2009;116:1604-9.
19. Pang Y, Frantz KA, Block S, Goodfellow GW, Allison C. Effect of amblyopia treatment on macular thickness in eyes with myopic anisometropic amblyopia. Invest Ophthalmol Vis Sci 2015;56:2677-83.
20. Yoon DH, Chun BY. Comparison of the thickness and volume of the macula and fovea in patients with anisometropic amblyopia prior to and after occlusion therapy. Korean J Ophthalmol 2018;32:52-8.
21. Tugcu B, Araz-Ersan B, Erdogan ET, Tarakcioglu H, Coskun C, Yigit U, *et al.* Structural and functional comparison of the persistent and resolved amblyopia. Documenta Ophthalmologica 2014;128:101-9.
22. Chen W, Chen J, Zhang F, Zhu X, Lu F. Visual outcome in isoametropic amblyopic children with high hyperopia and the effect of therapy on retinal thickness. Am J Ophthalmol 2013;155:536-43.
23. Kasem MA, Badawi AE. Changes in macular parameters in different types of amblyopia: Optical coherence tomography study. Clin Ophthalmol 2017;11:1407-16.