Evaluation of Retinal Nerve Fiber Layer and Macular Thickness in Amblyopia

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Abstract

**Purpose:** To investigate the differences in macular and nerve fiber layer thicknesses between amblyopic and fellow eyes.

**Method:** One hundred and twenty two eyes of 61 patients were enrolled for this study. All patients underwent complete ocular examination, cover test, prism test and also RNFL, macular thickness measurements (CMT; central macular thickness, TMT; total macular thickness) were obtained with OCT. 61 amblyopic (30 strabismic, 31 anisometropic) eyes and 61 fellow eyes were compared. A comparison of all amblyopic eyes versus fellow eyes was conducted. Amblyopic subgroups were also compared with both each other and fellow eyes, respectively.

**Results:** There was slightly elevated RNFL in strabismic group comparing to anisometropic group, but the difference was not significant. The strabismic group had both lower values in CMT and TMT than the anisometropic group but only the difference in TMT values was statistically significant (p: 0.043). Although the all amblyopic group had elevated RNFL, CMT and TMT values were lower comparing fellow eyes, but none of the differences were statistically significant.

**Conclusion:** The only significant result in our study between strabismic and anisometropic groups was TMT. The evaluation between amblyopes and fellow eyes revealed no differences. Amblyopia does not seem to have prominent effect on retinal structures.

Introduction

The meaning of the word Amblyopia is blurred vision (Amblyos: blurred, Opia: vision). Amblyopia is a disorder where visual acuity does not develop properly in one or both eyes during childhood. It is the most common cause for decreased vision in children with 1-5% [1].

Amblyopia can be associated with strabismus, anisometropia or disruption of normal development of the lateral geniculate body during the neonatal period [2]. In 1963 Wiesel and Hubel revealed that in infant cats and monkeys, deprivation of visual stimulation by suturing unilateral lid, induced anatomical and electrophysiological changes of the lateral geniculate body and the visual cortex [3].

It also has been suggested that abnormalities in the retinal ganglion cells may be attributable to the effect of amblyopia on the process of postnatal reduction of ganglion cells [4]. Red-free ophthalmoscopy, scanning laser polarimetry (SLP), and optical coherence tomography (OCT) can evaluate retinal nerve fiber layer (RNFL) and macular thickness. In several studies which were investigating the relationship between amblyopia and retinal anatomy, RNFL was found thicker comparing control patients [5,6]. On the other hand, in various studies, macular thickness was found elevated in amblyopic patients comparing to controls while in many studies no differences were found in RNFL and macular thickness between the amblyopic and healthy individuals [7-12].

There are many controversial results in literature about morphological changes in macular thickness and RNFL in amblyopic patients. The aim of our study is to investigate differences between amblyopic and fellow eyes in RNFL and macular thickness with OCT.

Material and Method

The study was conducted at department of ophthalmology at (**). 122 eyes of 61 patients (61 amblyopic eyes, 61 fellow eyes) were enrolled to the study. The amblyopic group consisted 31 anisometropic and 30 strabismic eyes. All patients underwent complete ocular examination including visual acuity, biomicroscopic examination, cover test, prism test, retinal examination using optical coherence tomography. The amblyopic eye was defined as an eye that has a visual acuity of at least two lines worse than the normal eye with Snellen chart, having no ocular problem in the visual axis such as leukemia or cataract or macular disease. Anisometropia was defined as a cycloplegic spherical equivalent difference greater than 2.00 diopters between fellow eyes.

We used Optical Coherence Tomography device from OPKO (Spectral OCT SLO, Opko, Florida USA) for measuring the thicknesses of the fovea and the retinal nerve fiber layer. The measurement of the fovea and the retinal nerve fiber layer thickness was performed by the same masked examiner (a doctor from our clinic). OCT images were obtained using spectral domain OCT after pupillary dilatation with 1% cyclopentolate hydrochloride. Two different values were noted about macula; central 1 mm diameter area was defined central macular thickness (CMT) and 6 mm diameter area is total macular thickness (TMT). RNFL scan was performed with three peripapillary scans with the protocol of having diameter of 3.4.
mm centered on the optic disc. The instrument software calculates average thickness values for two quadrants (superior, inferior) and average RNFL automatically.

Patients with systemic or ocular disease (glaucoma, leukemia) or had previous ocular surgery, nystagmus and patients with spherical equivalent difference smaller than 2.00 diopter were excluded from this study. Written informed consent was also obtained from each patient or their parents. The study was conducted with accordance of declaration of Helsinki.

Statistical analysis

The statistical analysis for the comparison of the fovea and the retinal nerve fiber layer thicknesses between the amblyopic eye and fellow (control) eye was performed using the T test. P values less than 0.05 were considered to be statistically significant. SPSS software version 21.0 (SPSS, Inc., Chicago, IL) was used for statistical analyses. Analysis of variance was used to compare the differences between the three groups. Sample T test was used to determine whether differences between values of the amblyopic eyes and nonamblyopic eyes were significant.

Results

Two major groups were compared in this study; amblyopic group and their fellow eyes (control). The amblyopic group included 61 eyes; 30 strabismic and 31 anisometropic. There were 15 boys and 15 girls in strabismic subgroup and 16 boys and 15 girls in anisometropic subgroup, respectively. The strabismic group contains 12 esotropic and 18 exotropic patients. The anisometropic group had 9 myopic and 22 hyperopic anisometropes. Mean ages were 13.5+2.12 (range 6-25) in the strabismic subgroup and 11.21+2.44 (range 7-15) in the anisometropic subgroup. There was no statistically significant difference in ages between those groups. The average visual acuity with Snellen charts in anisometropic group was 0.49 and 0.44 in strabismic subgroup, but neither of the differences were statistically significant. When comparing amblyopic subgroups eachother, the strabismic group had slightly thicker RNFL (106 µm) than control group but again, the difference was not statistically significant.

A total evaluation of all amblyopic subjects (anisometropic +strabismic) comparing to control group (104 µm), but CMT and TMT values were found smaller respectively. On the other hand, none of them were found significantly different (Table 2).

Comparing RNFL, CMT and TMT values between strabismic and control groups, but again, the difference was not statistically significant. When comparing central and total macular thickness, none of the differences were found statistically significant (Table 3).

Discussion

The reason of amblyopia is still certainly unknown. There are many possible causes that might promote for amblyopia development. It was possible causes that might promote for amblyopia development.

Table 1: Comparison of the two amblyopic subgroups eachother with central macular thickness, total macular thickness and RNFL values.

<table>
<thead>
<tr>
<th></th>
<th>Strabismic (n:30)</th>
<th>Anisometropic (n:31)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNFL µm</td>
<td>105.9000 ± 15.59918</td>
<td>102.4516 ± 14.43107</td>
<td>0.374</td>
</tr>
<tr>
<td>CMT µm</td>
<td>147.8667 ± 65.33296</td>
<td>151.8710 ± 67.68394</td>
<td>0.815</td>
</tr>
<tr>
<td>TMT µm</td>
<td>254.0667 ± 40.59041</td>
<td>276.8387 ± 45.00600</td>
<td>0.043</td>
</tr>
</tbody>
</table>

TMT: Total Macular Thickness; CMT: Central Macular Thickness; RNFL: Retinal Nerve Fiber Layer

Table 2: RNFL, CMT and TMT values in Strabismic group and fellow eyes.

<table>
<thead>
<tr>
<th></th>
<th>Strabismic (n:30)</th>
<th>Control (fellow eyes)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNFL µm</td>
<td>105.9000 ± 15.59918</td>
<td>104.1667 ± 13.75922</td>
<td>0.650</td>
</tr>
<tr>
<td>CMT µm</td>
<td>147.8667 ± 65.33296</td>
<td>151.6000 ± 53.88980</td>
<td>0.810</td>
</tr>
<tr>
<td>TMT µm</td>
<td>254.0667 ± 40.59041</td>
<td>262.7000 ± 27.56703</td>
<td>0.340</td>
</tr>
</tbody>
</table>

TMT: Total Macular Thickness; CMT: Central Macular Thickness; RNFL: Retinal Nerve Fiber Layer

Table 3: RNFL, CMT and TMT values in Anisometropic group and fellow eyes.

<table>
<thead>
<tr>
<th></th>
<th>Anisometropic (n:31)</th>
<th>Control (fellow eyes)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNFL µm</td>
<td>102.4516 ± 14.43107</td>
<td>103.0645 ± 12.69103</td>
<td>0.860</td>
</tr>
<tr>
<td>CMT µm</td>
<td>151.8710 ± 67.68394</td>
<td>162.9032 ± 63.10486</td>
<td>0.509</td>
</tr>
<tr>
<td>TMT µm</td>
<td>276.8387 ± 45.00600</td>
<td>269.5806 ± 23.11100</td>
<td>0.428</td>
</tr>
</tbody>
</table>

TMT: Total Macular Thickness; CMT: Central Macular Thickness; RNFL: Retinal Nerve Fiber Layer

Table 4: A comparison of RNFL, CMT and TMT values between amblyopic and control Groups.

<table>
<thead>
<tr>
<th></th>
<th>Amblyopic (n:61)</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNFL µm</td>
<td>104.1475 ± 14.99204</td>
<td>103.6066 ± 13.12793</td>
<td>0.832</td>
</tr>
<tr>
<td>CMT µm</td>
<td>149.9016 ± 66.01280</td>
<td>157.3443 ± 58.54254</td>
<td>0.511</td>
</tr>
<tr>
<td>TMT µm</td>
<td>265.6393 ± 44.05528</td>
<td>266.1967 ± 25.42428</td>
<td>0.932</td>
</tr>
</tbody>
</table>

TMT: Total Macular Thickness; CMT: Central Macular Thickness; RNFL: Retinal Nerve Fiber Layer

Table 4: A comparison of RNFL, CMT and TMT values between amblyopic and control Groups.
once considered as a situation associated with an abnormality of the retina [13]. However, amblyopia-induced cerebral changes were later shown in the visual cortex and the lateral geniculate body.

In 1977, von Noorden et al. reported that, several changes occurred after amblyopia development with suturing one lid, such as; an arrest in the lateral geniculate body cell growth, an abnormal distribution of the cerebral cortex, and a decrease in the size and density of parafoveal ganglion cells [14]. Wiesel and Hubel have reported that atrophy of the neurons in the cerebral cortex and lateral geniculate body was detected; nevertheless, it had no influence on the retina [3].

One of the major consequences of amblyopia is reduction in the ganglion cells and optic disc. Lempert et al. showed that in a presumed healthy population the RNFL thickness in amblyopic eyes [16]. In their study, the RNFL thickness in the normal eyes of the emmetropic subjects was not clinically significant comparing both anisometropic group and fellow eyes. Also, all amblyopic patients had slightly thicker RNFL comparing all controls. But none of the differences were not statistically significant. Similar to Yalcin et al., Altintas et al. and Firat et al., our study revealed no significant difference in RNFL between amblyopic and fellow eyes [8,18,10].

There is another region in retina that has been investigated with imaging devices in amblyopia. Macular thickness was also compared in amblyopic eyes and control groups. There are various results obtained from different studies in literature.

Another study performed by Yoon et al. used OCT to measure the peripapillary RNFL and foveal thickness in patients with anisometropic amblyopia. Even though RNFL in patients with amblyopia was found significantly thicker, there was no significant difference in macular thickness [6].

In another study, Xu et al. reported the fovea and the central sector of the retina in amblyopic eyes were slightly but not significantly thicker than those in the normal fellow eyes in children aged seven to 14 years [19]. Huynh et al. found increase in macular region among amblyopic patients but it was not statistically significant [20]. In another study Yalcin et al. reported that the mean foveal thickness for amblyopic patients was 220 ± 38.25 microns; for fellow eyes, it was 202.87 ± 31.01 microns, and for healthy subjects, 198.91 ± 22.50 microns. They found a statistical difference between groups (P=0.025). The difference between amblyopes and fellow eyes was statistically significant (P=0.038). There was also a significant statistical difference in macular thickness between amblyopes and healthy subjects (P=0.028) [8].

Tugcu et al. conducted similar study about amblyopic and control patients but they both evaluated persistent and resolved amblyopia. They found that foveolar thickness was significantly increased in both resolved and persistent amblyopia groups compared with the control group (p=0.031). However, there was no difference between amblyopic groups [21]. Al-Haddad et al. demonstrated that the mean macular thickness was significantly increased in amblyopic eyes versus the fellow eye while the mean the RNFL thickness was similar. The mean macular thickness was significantly increased in the amblyopic (273.8 μm) vs fellow eyes (257.9 μm) in their study (p=0.001). This difference remained significant in the anisometric group (p=0.002) but not the strabismic group [7].

In our study, we compared macular thickness of strabismic amblyopes, anisometropic amblyopes and fellow eyes. The anisometropic subgroup had slightly thicker macula, while the strabismic subgroup was thinner comparing their fellow eyes. When comparing all amblyopic patients to their fellow eyes, the mean macular thickness is 265 μm in amblyopic group and 266 μm in fellow eyes, respectively. But the difference was not significant (p=0.932).

Our study aimed to investigate to report the difference in RNFL and macular thickness between amblyopic and fellow eyes. OCT was used to obtain the data like other studies but the differences between devices and the examiners, the patients ages and their refractive errors. Our study did not obtain data from patients after they overcome amblyopia with treatment. The mechanism of amblyopia and the differences between normal eyes is not totally understood yet. Further studies, including histopathological and instrumental studies with a
greater number of patients, are required to investigate the differences between amblyopic and normal eyes.

References