Ganglion Cell-Inner Plexiform Layer Assessment with Cirrus Hd 5000 in Early Glaucoma

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Citation

Abstract
This study aims to assess the effectiveness of ganglion cell-inner plexiform layer (GCIPL) measurements in preperimetric glaucoma (PPG) and primary open angle glaucoma (POAG). GCIPL and retinal nerve fiber layer (RNFL) thickness were measured in PPG, POAG, and control groups. The data obtained from these three groups were compared with analysis of variance and post hoc Tukey test. Average GCIPL was 70.99±11.02 µm in PPG group, 68.95±11.93 µm in POAG group, and 84.77±9.75 µm in control group. (p< 0.001). Average RNFL was 76.16±16.55 µm in PPG group, 70.33±21.02 µm in POAG group, and 98.13±11.48 µm in control group (P< 0.001).

Pearson correlation coefficient between GCIPL and RNFL was r=0.59 (p<0.05) in POAG group, and r=0.51 (p<0.05) in PPG group. In conclusion, macular GCIPL thickness significantly decreases in PPG and POAG and this is correlated with RNFL decrease.

1. Introduction

Glaucoma is a multifactorial optic neuropathy with progressive retinal ganglion cell and nerve fiber layer loss, of which intraocular pressure (IOP) is an important etiologic factor (1). Early diagnosis and preventing visual loss is challenging because of asymptomatic presentation in early period of primary open-angle glaucoma (POAG). Early diagnosis and treatment is essential because untreated glaucoma leads to irreversible visual loss. Cupping and atrophy of the optic nerve in the glaucoma are caused by progressive ganglion cell loss. This is accompanied by typical visual field (VF) defects. However, since vision loss occurs after serious neuronal loss, it is not only a matter of assessing visual field losses but also needs further investigations. Optical coherence tomography (OCT), optic nerve morphology and peripapillary nerve fiber layer (RNFL) thickness measurements are important in glaucoma diagnosis and follow-up (2). New generation spectral OCT devices those have the ability of even five µm sensitivity are gaining importance in glaucoma diagnosis. Recently, OCT device softwares have allowed ganglion cell-inner plexiform layer (GCIPPL) thickness measurement. In this study, comparison of GCIPL measurements in POAG, preperimetric glaucoma (PPG) and normal cases was aimed.
2. Method

PPG and POAG patients referred to ophthalmology clinic in 2017 were included in this study. A control group were made up with patients without glaucoma. Approval of Medipol University Ethics Committee has been obtained. The study was carried out in accordance with the Helsinki Human Rights Declaration and the informed consent was obtained from the patients. Three groups were formed. PPG group included the patients with IOP > 21 mm.Hg, normal visual field, and glaucomatous optic nerve or RNFL changes. Glaucoma group included the patients with IOP > 21 mm.Hg, glaucomatous visual field changes, corresponding RNFL changes, and optic nerve changes. Control group included the patients with IOP < 21 mm.Hg and no glaucomatous optic nerve, VF, and RNFL changes. Patients with secondary glaucoma, hazy optical media, high refractive errors (> six diopters), retinal diseases that would affect VF and RNFL measurements, active ocular infection or inflammation were excluded from the study. Best spectacle corrected visual acuity (BSCVA), IOP, anterior segment slit-lamp examination, gonioscopic examination of the anterior chamber angle, fundus examination, VF analysis, RNFL and optic nerve head analysis with spectral OCT (Cirrus HD 5000, Zeiss, Germany) were performed in all patients. IOP measurement was made with applanation tonometer. IOP value was corrected according to Ehler’s correction table based on central corneal thickness and recorded for statistical data (1). RNFL and optic nerve head analysis were performed with optic disc cube 200x200 test and macular ganglion cell analysis was performed with macular cube 512x128 test in Cirrus HD 5000 OCT. Measurements with a signal level below 6/10 were not taken into account. Computerized VF examination was performed with the Humphrey 30-2 Sita-standard method.

The data was saved as a Microsoft Excel file. Statistical analysis was performed with StatPlus 9.0 (Analysoft, USA) statistical software. Comparison of three groups was made with ANOVA test. Comparisons between groups were made by post hoc Tukey test. Two tailed distribution outcomes were accepted for P values. P values < 0.05 were considered to be statistically significant.

3. Results

Fifty-one eyes of 51 patients were included in the study. The mean age was 55.48 ± 14.02 in PPG group, 57.15 ± 13.74 in the POAG group and 54.37 ± 15.4 years in the control group (p = 0.214). Patients were 47% female and 53% male in the preperimetric group; 51% female and 49% male in the glaucoma group; 46% female and 54% were male in the control group (p = 0.756).

There was a statistically significant difference in mean RNFL, inferior quadrant RNFL, GCIPL and rim area value between PPG, glaucoma and control groups (ANOVA, Table 1). In post-hoc Tukey tests, the difference between PPG and control; and the difference between POAG and control groups were significant (Table 2). The correlation between GCIPL and RNFL was statistically significant in the POAG group (r = 0.59, p <0.05) and the PPG group (r = 0.51, p <0.05).

Table 1. Comparison of three groups in terms of RNFL, GCIPL, Inferior RNFL ve rim area.

<table>
<thead>
<tr>
<th>Mean ± s. d</th>
<th>PPG (n=17)</th>
<th>POAG (n=17)</th>
<th>Kontrol (n=17)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNFL (µm)</td>
<td>76.16±16.55</td>
<td>70.33±21.02</td>
<td>98.13±11.48</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>GCIPL (µm)</td>
<td>70.99±11.02</td>
<td>68.95±11.93</td>
<td>84.77±9.75</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Inferior RNFL (µm)</td>
<td>71.14±14.51</td>
<td>64.16±10.28</td>
<td>90.36±13.52</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Rim area (mm²)</td>
<td>0.77±0.43</td>
<td>1.07±0.54</td>
<td>1.48±0.67</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

Table 2. Comparison of glaucoma groups and control group with Post hoc Tukey test.

<table>
<thead>
<tr>
<th>P value</th>
<th>PPG - Control</th>
<th>POAG - Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNFL (µm)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>GCIPL (µm)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Inferior RNFL (µm)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Rim area (mm²)</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
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</tbody>
</table>

RNFL, BGA, and GCIPL outcomes of a PPG patient with GCIPL thinning and rim area loss despite normal VF in right eye are shown in figure 1, 2, 3.
Figure 1. RNFL of a PPG patient. Rim area loss in right eye.
Figure 2. BGA of the same patient (right eye).
4. Discussion

Glaucoma is a multifactorial optic neuropathy characterized with loss of ganglion cells and axons [2]. The presence of glaucomatous visual field defects is an important part of the diagnosis just as clinical findings. Quantitative evaluation of retinal nerve fiber layer thickness and optic nerve parameters became possible after use of OCT devices.

Thus, early assessment of nerve fiber loss has been possible in patients with PPG who had yet no visual field loss. Selective early ganglion cell loss is seen in the course of the glaucoma. Approximately 50% of ganglion cells are clustered in macula. [3, 4]. Different Inner retinal thickness profiles have been developed by OCT device manufacturers. Optovue SD-OCT has ganglion cell complex analysis which includes ganglion cell layer, inner plexiform layer, and retinal nerve fibre layer. Nerve fibre layer refers to axons of...
the ganglion cells, whereas inner plexiform refers to dendritic extensions. The Cirrus HD 5000 OCT can quantitatively assess the inner plexiform and ganglion cell layers in the macula area. Heidelberg measures the whole retinal thickness in contrast to other OCT devices, and performs a macular retinal thickness asymmetry analysis for glaucoma diagnosis.

Recently, studies have reported that the evaluation of macular GCIPL might have an important place in glaucoma diagnosis. Kim et al. reported that ganglion cell layer measurements were reliable as peripapillary RNFL measurements in glaucoma diagnosis [5]. Tiryaki et al. reported that the loss of GCIPL and RNFL were correlated with loss of visual field and electroretinography values in POAG patients [6]. Cennamo et al. reported that GCIPL measurements were more reliable than RNFL measurements in PPG diagnosis [7]. Chien et al. reported that measurements of GCIPL and isolated ganglion cell layer were reliable in the diagnosis of glaucoma, but the isolated inner plexiform layer measurement was not equally reliable [8]. Hollo et al. reported that there was loss of > 1.3 µm / year in GCIPL and > 1.5 µm / year in RNFL layers in patients with ongoing treatment for ocular hypertension [9]. Harwerth et al. showed correlation between ganglion cell loss and visual field loss in the experimental animal models (10). Le et al reported macular GCIPL thickness assessment to be useful in the early diagnosis of PPG [11]. Kita et al. reported that GCIPL / outer retina thickness rate might be more useful compared to merely GCIPL thickness measurement [12]. Azusa et al. reported GCIPL measurement to be more effective than RNFL measurement [13]. Sung et al. reported taking into account GCIPL measurement in evaluating RNFL to be more effective in the early diagnosis of PPG and POAG [14]. Considering the sectoral GCIPL measurements instead of the average GCIPL thickness of the macula increases the diagnostic sensitivity [15]

5. Conclusion

In this study, Both RNFL and GCIPL thicknesses were found to be significantly reduced in PPG and PAAG patients compared to the control group. This is consistent with the studies mentioned above. One of the limitations of this study is its cross-sectional design and does not give information about glaucoma progression. Limited number of cases is another limitation. In this study VF is used to distinguish PPG, PAAG and healthy cases and evaluation of the correlation between GCIPL loss and VF findings needs further prospective studies. In conclusion, according to the results of this study, macular GCIPL thickness significantly decreases in PPG and POAG and this is correlated with RNFL decrease.

References


