Purpose: To test whether pattern electroretinogram (PERG) can early detect retinal ganglion cells dysfunction in ocular hypertension.

Design: Cross-sectional observational study.

Participants: The study included 3 groups: control, primary open-angle glaucoma (POAG) and ocular hypertension (OHT) groups with 30 eyes in each group.

Materials and Methods: Visual fields were examined using automated perimetry with central 24-2 program. Optical coherent tomography (OCT) was done to assess the neuroretinal rim area, vertical cup/disc ratio, and average superior and inferior retinal nerve fiber layer thickness. PERG was recorded using skin electrodes. Amplitude and latency of P50 and N95 were documented.

Results: PERG data: the mean P50 and N95 latency were significantly higher in the POAG group and the OHT group compared with the control group (P < 0.001, <0.001, respectively). Also, the mean P50 and N95 amplitude were significantly lower in the POAG group and the OHT group compared with the control group (P < 0.001, <0.001, respectively). In the POAG group, there was a significant negative correlation between PSD on one hand and P50 amplitude (r = −0.620, P = 0.001) and N95 amplitude (r = −0.61, P < 0.001) on the other hand. Also, the mean deviation was positively correlated with P50 amplitude (r = 0.51, P = 0.007) and N95 amplitudes (r = 0.50, P = 0.002). However, there was no significant correlation between PERG parameters and OCT parameters. In the OHT group, PERG parameters did not correlate with visual field and OCT parameters.

Conclusions: PERG can detect the dysfunctional, but still live retinal ganglion cells earlier than OCT in OHT cases, allowing the early start of treatment that can restore the ganglion cell function before irreversible damage occurs.

Key Words: pattern electroretinogram, retinal ganglion cells, optical coherent tomography, primary open-angle glaucoma, ocular hypertension

C

Glaucoma is an optic neuropathy characterized by a compromise in the communication between the retinal ganglion cell (RGC) axon and body leading to necrosis or apoptosis of these cells while the photoreceptors and bipolar cells remain nearly normal.1 Progressive degeneration of RGCs results in optic disc cupping and visual field (VF) loss.2 Ocular hypertension (OHT) is considered as the most important risk factor for glaucoma and lowering the intraocular pressure (IOP) is the most effective way to prevent glaucoma progression.3–5 Diagnostic techniques are needed to detect RGC damage at an earlier stage of the disease and select the appropriate time to start treatment to prevent occurrence of irreversible VF defects.6 Although standard automated perimetry (SAP) is the gold standard in diagnosis and follow-up of glaucoma patients, it may not detect defects if <40% of the ganglion cell axons are damaged.7,8 Larger number of early glaucoma patients can be detected by optical coherent tomography (OCT) than SAP. The hypothesis of “RGC functional reserve or redundancy” in early glaucoma suggested that the structural damage precedes functional loss because of a curvilinear relationship between function and structure and changes can only be detected by OCT in the preperimetric stage of glaucoma. In contrast to this hypothesis, it has been suggested that there is a disease stage in which dysfunction of RGC precedes cellular and axonal loss resulting in functional losses in the presence of a normal structure and can only be detected by pattern electroretinogram (PERG).9,10 Moreover, in ocular hypertension, there are no VF changes and OCT does not demonstrate clear RGC loss and cannot tell which cases are indicated for treatment.11,12 This role of PERG is supported by the results of Ventura and Porciatti documenting restoration of RGC function, detected by PERG improvement, after IOP reduction in glaucomatous eyes with early VF impairment.13 In addition to the results of the study by Parisi et al13 who found abnormal PERG amplitudes in 69.12% of the OHT eyes and 100% of the OAG patients.

The aim of this study is to test whether PERG can early detect RGCs dysfunction in ocular hypertension. PERG parameters regarding P50, N95 latency, and amplitude in cases of OHT and primary open-angle glaucoma (POAG) were documented and compared with control and correlated to VF, OCT parameters.

MATERIALS AND METHODS

This cross-sectional observational study included 90 eyes of 90 participants with ages ranging from 40 to 60 years. They were recruited from Memorial Institute of Ophthalmic Research, Giza, Egypt, starting from July 2016 for 17 months. The study was approved by the Institutional Review Board and was conducted in compliance with the Helsinki declaration. A written consent form was obtained from all patients.

The participants were divided into 3 groups. The control group included 30 normal eyes of 30 subjects having an IOP of <21 mm Hg, normal VF with an MD of >–2 dB
and PSD with \( P > 0.05 \) and clinically normal optic disc on slit-lamp biomicroscopy having a vertical C/D not > 0.6, with no C/D ratio asymmetry ≥ 0.2, optic disc excavation, thinning of the neuroretinal rim, notching or peripapillary splinter hemorrhages. The POAG group included 30 eyes of 30 patients with an IOP documented > 21 mm Hg measured on 2 separate occasions having at least one of the above mentioned glaucoma optic disc signs and repeatable glaucomatous VF with an MD of < −2 dB and PSD with \( P < 0.05 \) have mild to moderate glaucoma (according to HODAPP classification of VF)\(^{14} \) and controlled with medical treatment; Dorzolamide 2% + Timolol 0.5% (combination eye drop), Latanoprost 0.005%, or both medications. All enrolled POAG cases had an IOP below 16 mm Hg at the time of PERG recording and have been controlled for at least 1 year before the time of the study. The OHT group included 30 eyes of 30 patients having similar criteria to the control group except an IOP > 21 mm Hg measured on 2 separate occasions. All included cases had to have central corneal thickness between 520 and 560 \( \mu \)m measured by Scheimpflug camera (Oculus Optikgerate GmbH, Wetzlar, Germany).

The following conditions were excluded: closed-angle glaucoma, childhood glaucomas, secondary glaucomas, previous ocular laser or surgery, diabetes mellitus, myopia > 6 diopters that may induce VF changes, macular disorders affecting RGCs (eg, macular edema and macular dystrophies) or neurologic disorders that may affect the VF. We excluded OHT and POAG cases that received any of the following drugs: Coenzyme Q10, Nicergoline, or Citicoline which are known to improve the PERG response.\(^{15-21} \)

All cases underwent ophthalmic examination including IOP measurement using Goldmann applanation tonometry, slit-lamp biomicroscopy with 90 diopter lens, and anterior chamber angle assessment using a gonio-3 mirror lens. VF examination was done using an automated perimeter (Humphrey, Carl Zeiss Meditec Inc., Dublin, CA). The central 24-2 program was selected using the standard protocol SITA (Swedish interactive threshold algorithm). All of the VF tests had to have a fixation loss, false-positive and false-negative response rates of <20% to be considered reliable. OCT was done using 3D OCT-2000 FA plus (version 8.11, spectral domain OCT, Topcon, Japan) to assess the optic nerve head criteria including neuroretinal rim area in \( \text{mm}^2 \), vertical C/D ratio, and average superior and inferior retinal nerve fiber layer (RNFL) thickness in \( \mu \)m.

PERG was recorded binocularly (using Reti-com system, Roland Consult, Germany). PERG measurements were conducted using Dawson-Trick-Litzkow electrodes according to the International Society for Clinical Electrophysiology of Vision standards.\(^{22} \) The active electrode was placed on the medial epicanthus whereas the reference electrode was placed in the temporal region of the same eye 2 cm from the eye. The ground electrode was placed on the forehead. Patients’ viewing distance was 50 cm from the screen using reading glasses. Recordings were done while looking binocularly at a fixation point on the screen. A checkerboard pattern of 95% contrast black and white with 0.8 degree checks in a 15-degree field was used for PERG measurements. The contrast reversing frequency was 2 Hz and the analog filter was between 0.03 and 100 Hz. Care was taken that the impedance remained under 8 kOhm. A total of 100 repeats were averaged. The data obtained were filtered between 1 and 50 Hz. Artifacts in the data due to eye movements were eliminated. All electrophysiology traces were characterized by 2 negative and 1 positive deflection in the order N35, P50, and N95. Amplitude and latency of P50 and N95 were recorded. The P50 amplitude is measured from the trough of N35 to the peak of P50, whereas the N95 amplitude is measured from the peak of P50 to the trough of N95.

Clinical examination and VF for all cases were done by a single ophthalmology specialist (E.T.), whereas OCT and PERG were done by a single trained operator (M.H.O.).

### The Statistical Methods

The data were statistically described as mean ± SD, median, range, frequencies, or percentages when appropriate. The comparison of numerical variables between the study groups was made using 1-way analysis of variance test with post hoc multiple 2-group comparisons. Within-group comparison of numerical variables was made using paired \( t \) test. Correlation between various variables was done using Pearson product-moment correlation equation for linear relation of normally distributed variables and Spearman-rank correlation equation for nonnormal variables/non-linear monotonic relation. A \( P \)-value < 0.05 was considered statistically significant. In case of multiple comparisons, Bonferroni adjustment was used. Sample size was calculated according to PERG amplitudes. Effect size of PERG was calculated by Hedge G. Effect; size is considered very small.

| Table 1. Demographic and Clinical Data of the 3 Studied Groups |
|-----------------|-----------------|-----------------|
| Control Group  | POAG Group      | OHT Group       |
| Age (y)         | 48.6 ± 4.4      | 52.1 ± 9.6      | 43.4 ± 2.0      |
| Percentage of males (%) | 66                  | 80                  | 73                  |
| Snellen BCVA (decimal) | 0.94 ± 0.11      | 0.70 ± 0.17      | 0.86 ± 0.16      |
| Intraocular pressure (mm Hg) | 13.3 ± 2.0      | 14.0 ± 2.2      | 24.4 ± 1.1      |
| (Goldmann applanation)               |

Data are expressed as mean ± SD. BCVA indicates best corrected visual acuity.

| Table 2. The Visual Field Data of the 3 Studied Groups |
|-----------------|-----------------|-----------------|
| Control Group   | POAG Group      | OHT Group       |
| MD (dB)         | −0.94 ± 0.73    | −6.03 ± 2.48    | −1.14 ± 0.70    |
| PSD (dB)        | 1.54 ± 0.33     | 5.49 ± 2.88     | 1.65 ± 0.26     |

Data are expressed as mean ± SD.

\( P \)-value

- \( P1 \): Control versus POAG
- \( P2 \): Control versus OHT
- \( P3 \): POAG versus OHT

MD indicates mean deviation; PSD, pattern standard deviation.

* \( P \) is significant if < 0.05 (1-way analysis of variance test, with post hoc multiple 2-group comparisons).
TABLE 3. OCT Findings in the 3 Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Control Group</th>
<th>POAG Group</th>
<th>OHT Group</th>
<th>$P_1$</th>
<th>$P_2$</th>
<th>$P_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertical C/D ratio</td>
<td>0.54 ± 0.09</td>
<td>0.64 ± 0.11</td>
<td>0.58 ± 0.07</td>
<td>0.001*</td>
<td>0.489</td>
<td>0.040*</td>
</tr>
<tr>
<td>Average superior RNFL thickness (μm)</td>
<td>116.9 ± 7.2</td>
<td>105.0 ± 14.9</td>
<td>115.8 ± 26.3</td>
<td>0.063</td>
<td>0.999</td>
<td>0.650</td>
</tr>
<tr>
<td>Average inferior RNFL thickness (μm)</td>
<td>124.2 ± 8.3</td>
<td>105.1 ± 16.8</td>
<td>121.0 ± 22.6</td>
<td>&lt;0.001*</td>
<td>0.999</td>
<td>0.001*</td>
</tr>
<tr>
<td>Rim area (mm²)</td>
<td>1.77 ± 0.32</td>
<td>1.44 ± 0.48</td>
<td>1.75 ± 0.53</td>
<td>0.020*</td>
<td>0.999</td>
<td>0.037*</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD.

$P_1$: control vs. POAG, $P_2$: control vs. OHT, $P_3$: POAG vs. OHT.

RNFL indicates retinal nerve fiber layer; vertical C/D ratio, vertical cup/disc ratio.

* $P$ is significant if <0.05 (1-way analysis of variance test, with post hoc multiple 2-group comparisons).

RESULTS

Table 1 shows the mean ± SD of demographic and clinical data of the 3 groups. Table 2 shows the mean ± SD of VF data of the 3 groups. In the POAG group, the mean deviation was significantly lower and the PSD was significantly higher than the other 2 groups. Table 3 shows OCT findings in the 3 groups. The mean of vertical cup/disc (C/D) ratio was significantly higher in the POAG group compared with the control group ($P=0.001$) and OHT group ($P=0.040$). The mean inferior RNFL thickness was significantly lower in the POAG group compared with the control group ($P<0.001$) and OHT group ($P=0.001$). The mean rim area was significantly smaller in the POAG group compared with the control group ($P=0.02$) and OHT group ($P=0.037$). There is no statistically significant difference between control and OHT groups regarding all OCT findings.

In control group, average inferior RNFL thickness was significantly higher than average superior RNFL thickness ($P<0.001$). On the other hand, there were no significant differences between average superior and inferior RNFL thickness in POAG and OHT groups ($P=0.983$, 0.128, respectively).

Table 4 shows PERG findings in the 3 groups. The mean P50 and N95 latency were significantly higher in the POAG group and the OHT group compared with the control group ($P<0.001$, <0.001, respectively). Also, the mean P50 and N95 amplitude were significantly lower in the POAG group and the OHT group compared with the control group ($P<0.001$, <0.001, respectively). Table 5 shows the effect size of PERG parameters as calculated by Hedge G.

Correlations

Tables 6 and 7 show correlations between PERG parameters on one hand and the VF and OCT parameters on the other hand in POAG and OHT groups. In the POAG group, there was significant negative correlation between PSD on one hand and P50 amplitude ($r=-0.620$, $P=0.001$) and N95 amplitude ($r=-0.61$, $P<0.001$). Also, the mean deviation was positively correlated with P50 amplitude ($r=0.51$, $P=0.007$) and N95 amplitudes ($r=0.50$, $P=0.002$). However, there was no significant correlation between PERG parameters and OCT parameters. In the OHT group, PERG parameters did not correlate with VF and OCT parameters.

DISCUSSION

Early diagnosis of glaucoma is important for the prevention of irreversible VF defect. PERG is suggested to detect an earlier disease stage where RGC dysfunction occurs preceding cellular and axonai numerical loss. The aim of this study was to compare PERG findings in control, OHT, and POAG cases and to detect whether there is a correlation between PERG on one hand and VF and OCT on the other hand to assess the efficacy of PERG in detecting abnormality in OHT stage and select cases that benefit from treatment knowing that patients with increased IOP are considered as glaucoma suspects.

As it is well known that the IOP lowering may improve PERG responses,1–3,23,24 it should be considered that POAG cases enrolled in our study had IOP <16 mm Hg at the time of PERG recording and have been controlled for at least 1 year before the study while OHT cases are on no treatment. All POAG and OHT cases were not submitted to argon laser trabeculoplasty or surgical treatment. In addition, as in POAG, the PERG responses can be improved by Coenzyme Q10, Nicergoline or Citicoline treatment,15–21

TABLE 4. PERG Findings in the 3 Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Control Group</th>
<th>POAG Group</th>
<th>OHT Group</th>
<th>$P_1$</th>
<th>$P_2$</th>
<th>$P_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>P50 latency (ms)</td>
<td>50.4 ± 3.1</td>
<td>65.4 ± 2.5</td>
<td>63.9 ± 2.0</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.993</td>
</tr>
<tr>
<td>P50 amplitude (μV)</td>
<td>3.5 ± 0.9</td>
<td>1.5 ± 0.8</td>
<td>1.8 ± 0.9</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.644</td>
</tr>
<tr>
<td>N95 Latency(ms)</td>
<td>92.1 ± 5.6</td>
<td>102.7 ± 11.0</td>
<td>103.1 ± 9.7</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.999</td>
</tr>
<tr>
<td>N95 amplitude (μV)</td>
<td>5.8 ± 1.6</td>
<td>2.1 ± 0.8</td>
<td>2.3 ± 0.8</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.999</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD.

$P_1$: control vs. POAG, $P_2$: control vs. OHT, $P_3$: POAG vs. OHT.

* $P$ is significant if <0.05 (1-way analysis of variance test, with post hoc multiple 2-group comparisons).
we excluded OHT or POAG cases who received any of these drugs.

Some authors recommended the use of PERG checkboard pattern with check size of 0.8 degree for diagnosis of glaucomatous damage and the ratio between PERG amplitudes with check sizes of 0.8 and 16 degrees were also used,\(^25\)–\(^28\) whereas many others used visual stimuli with higher spatial frequency (ie, 1.7 cycle/degree or 15 minutes of visual arc) for more specific PERG responses in OHT and POAG cases.\(^1,9,13,29\) We selected check size of 0.8 degree according to the International Society for Clinical Electrophysiology of Vision standards.\(^22\)

It has been published in literature that the OCT ganglion cell layer and ganglion cell complex (GCC) have high discriminating ability of diagnosis of early glaucoma.\(^32\) Moreover, the PERG with a stimulus field of 15 degrees covers the macular area having the highest concentration of RGCs.\(^33,34\) However, many other papers reported that RNFL and optic nerve head parameters have equal diagnostic ability to GCC\(^11,35\) or even better.\(^36,37\) Many articles studying PERG value have used RNFL thickness for correlations.\(^9,29–31\) So, in this study, we selected RNFL and optic nerve head parameters as they represent all the ganglion cell axons whereas GCC represents only the macular area.\(^35\)

In the current study, OCT parameters of optic disc and RNFL, except average superior RNFL thickness, were significantly affected in POAG patients having significantly higher mean vertical C/D ratio and significantly lower mean rim area and inferior RNFL thickness compared with healthy controls and OHT patients. Meanwhile, OCT criteria were comparable in OHT patients and healthy controls. This is explained by the absence of optic disc and RNFL abnormalities in OHT cases. However, the current results demonstrated significantly thicker average inferior RNFL thickness compared with superior RNFL thickness in the control group (\(P < 0.001\)). This was not found in the POAG and OHT groups (\(P = 0.983\) and 0.128, respectively). This may be diminished average inferior RNFL thickness in POAG and OHT affecting the characteristic configuration of neuroretinal rim found in normal eyes, known as the ISNT rule, being broadest in the inferior rim, followed by the superior and nasal rims, and thinnest in the temporal disc region.\(^38\)

In this study, PERG yielded different results from those of OCT. Significantly higher latencies and lower amplitudes of P50 and N95 were found in both the POAG and OHT groups compared with the control group. Consequently, we concluded that PERG detected ganglion cells impaired response in some of OHT patients that were not evident in the VF or OCT. These results are supported by many studies. In a study by O’Donaghe and colleagues, OHT established glaucoma and control groups were followed for 2 years by clinical examination and PERG. They reported that PERG could distinguish established glaucomatous eyes from controls and the amplitudes of the PERG waves were reduced as the degree of clinical abnormality increased. They also found PERG abnormalities in some OHT eyes especially the higher risk ones.\(^10\) Bach et al\(^25\) reported that PERG can help to predict which cases of OHT will convert into glaucoma at least 1 year before conversion and it can be used to select cases indicated for preventative treatment and thus avoid unnecessary treatment for those who are not at risk. The same results were reported in a study done by Pfeiffer et al.\(^26\) Ventura and colleagues found, in glaucoma suspects and early glaucoma cases, that reduction in RGC electrical activity, exceeded the amount expected from lost RGC axons. So, they recommended the use of PERG in addition to OCT to detect reduced function of viable RGC.\(^27\) Both studies by Falsini and colleagues and Demir and colleagues found that the mean PERG amplitude was decreased in both OHT and early glaucoma patients compared with controls, although the mean RNFL thickness was reduced only in early glaucoma patients compared with both the OHT and control groups. They recommended using PERG amplitude analysis to detect dysfunction of ganglion cells in patients with OHT earlier than OCT.\(^9,39\)

In this study, the effect size of PERG parameters was calculated by Hedge G which is like Cohen D, but corrected for small sample size. It gives an indication of how good a given measure can differentiate groups. The effect sizes for the comparisons control versus POAG and control versus OHT were all between very large and huge. That is very good discrimination. For the comparison OHT versus POAG, the effect sizes were small to medium which is not so

### TABLE 6. Effect size of PERG Parameters as Calculated by Hedge G

<table>
<thead>
<tr>
<th>Parameter</th>
<th>C/POAG (r)</th>
<th>C/OHT (r)</th>
<th>OHT/POAG (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P50 latency</td>
<td>0.23</td>
<td>0.39</td>
<td>-0.09</td>
</tr>
<tr>
<td>P50 amplitude</td>
<td>0.18</td>
<td>0.31</td>
<td>0.19</td>
</tr>
</tbody>
</table>

r: correlation coefficient.
RNFL indicates retinal nerve fiber layer.
*P is significant if <0.05 (Pearson test).
TABLE 7. Correlation Between PERG Parameters on One Hand and Visual Field and OCT Parameters on the Other Hand in the OHT Group

<table>
<thead>
<tr>
<th></th>
<th>P50 Latency</th>
<th></th>
<th>P50 Amplitude</th>
<th></th>
<th>N95 Amplitude</th>
<th></th>
<th>N95 Latency</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P</td>
<td>r</td>
<td>P</td>
<td>r</td>
<td>P</td>
<td>r</td>
<td>P</td>
</tr>
<tr>
<td>Mean deviation</td>
<td>0.06</td>
<td>0.63</td>
<td>0.17</td>
<td>0.22</td>
<td>−0.003</td>
<td>0.55</td>
<td>0.09</td>
<td>0.87</td>
</tr>
<tr>
<td>Pattern SD</td>
<td>0.02</td>
<td>0.97</td>
<td>−0.13</td>
<td>0.81</td>
<td>−0.19</td>
<td>0.15</td>
<td>−0.39</td>
<td>0.18</td>
</tr>
<tr>
<td>Rim area</td>
<td>0.08</td>
<td>0.79</td>
<td>−0.28</td>
<td>0.37</td>
<td>−0.24</td>
<td>0.54</td>
<td>0.23</td>
<td>0.25</td>
</tr>
<tr>
<td>Inferior RNFL thickness</td>
<td>−0.11</td>
<td>0.92</td>
<td>0.03</td>
<td>0.48</td>
<td>0.23</td>
<td>0.25</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

r: correlation coefficient.
RNFL indicates retinal nerve fiber layer.

FIGURE 1. Representative cases of normal, POAG and OHT. Control VF: MD = −1.30 dB and PSD = 1.32 dB. POAG VF: MD = −11.71 dB (P < 0.5) and PSD = 6.58 dB (P < 0.5). OHT VF: MD = −0.52 dB and PSD = 1.69 dB. Control OCT: vertical C/D ratio, 0.47; average superior RNFL thickness, 120 µm; average inferior RNFL thickness, 122 µm; and rim area, 1.78 mm². POAG OCT: vertical C/D ratio, 0.84; average superior RNFL thickness, 76 µm; average inferior RNFL thickness, 95 µm; and rim area, 0.63 mm². OHT OCT: vertical C/D ratio, 0.6; average superior RNFL thickness, 120 µm; average inferior RNFL thickness, 125 µm; and rim area, 0.96 mm². Control PERG: P50 latency, 53.5 ms; P50 amplitude, 5.28 µV; N95 latency, 95.1 ms; N95 amplitude, 8.66 µV. (vertical scale, 5 µV/division and horizontal scale, 20 ms/division). POAG PERG: P50 latency, 69 ms; P50 amplitude, 1.22 µV; N95 latency, 89 ms; and N95 amplitude, 1.52 µV. (vertical scale, 1 µV/division and horizontal scale, 20 ms/division). OHT PERG: P50 latency, 65 ms; P50 amplitude, 1.42 µV; N95 latency, 99 ms; and N95 amplitude, 0.985 µV. (vertical scale, 1 µV/division and horizontal scale, 20 ms/division). OCT indicates optical coherent tomography; OHT, ocular hypertension; PERG, pattern electroretinogram; POAG, primary open-angle glaucoma; RNFL, retinal nerve fiber layer; VF, visual field. Figure 1 can be viewed in color online at www.glaucomajournal.com.
useful in discrimination. It is interesting that the P50 latency had such high values for the comparison control versus OHT. So we can depend on this parameter in such discrimination.

We found no significant correlation between the VF and PERG parameters in OHT group because the RGC dysfunction at this disease stage can only be detected using PERG, while the VF is still within normal. In POAG group, including mild and moderate glaucoma cases, the VF defects represent the combined effect of dysfunctional viable and nonviable RGC that exceeded the threshold for SAP to detect the disease. So, we found significant moderate correlation between the VF and PERG parameters; the increase in PSD and the decrease in MD were accompanied by a reduction in PERG amplitudes. The degree of correlation is expected to become stronger with more advanced disease stages with loss of more dysfunctional RGCs. Our results are similar to those by Parisi et al who reported significant correlation between PERG and VF parameters in OAG cases but no correlation found in OHT cases.

In the present study, there was no correlation between the OCT parameters and PERG findings in the OHT group denoting lack of structure-function relationship in this disease stage where RGC dysfunction detected by PERG was not accompanied yet by RNFL loss. Similarly, no correlation found between the same parameters in early and moderate POAG, although abnormal RNFL thickness was detected, but it is still lagging behind the reduction in RGC function detected by PERG, in addition to glial remodeling occurring in early glaucoma affecting OCT measurements. This correlation may be established in more advanced glaucoma stages.

There is great controversy in results of similar papers. Ventura et al reported that PERG amplitude correlated weakly with RNFL thickness in glaucoma suspects and no correlation found in early glaucoma cases suggesting weak structure-function relationship in this stage owing to the presence of a PERG-detected RGC dysfunction without any measurable damage to nerve axons. Falsini et al documented that PERG amplitude did not correlate with RNFL in OHT cases although there was positive correlation in early glaucoma cases suggesting lack of structure-function relationship in OHT and that relationship is established in early glaucoma. Two studies by Parisi et al reported a significant correlation between PERG parameters (including P50 to N95 amplitude and P50 latency) and RNFL thickness in OHT eyes and in OAG eyes. Jung et al reported a significant correlation between RNFL thickness and N95 amplitude in glaucoma patients. Cvenkel et al found a significant correlation between RNFL thickness and P50 amplitude in early glaucoma. This variability in results may be due to differences in PERG visual stimuli and recording parameters used in different studies. Also, the location of the VF defects in early glaucoma may have an impact on PERG being more affected with paracentral field defect than peripheral nasal defects. But the overall conclusion supports the hypothesis that the earlier the stage of the disease, the less the correlation between PERG and OCT and this correlation is established at certain more advanced stage.

Our study is limited by the small number of cases which did not allow multivariate analysis to be done, but fixing the recording parameters and comparing results to control group may increase the validity of our results. IOP of POAG cases enrolled in this study was medically controlled, so PERG may give different results if recorded in uncontrolled cases. Further studies with larger sample size can be done to compare PERG parameters in controlled and untreated POAG cases to detect the effect of IOP reduction. PERG correlation with RNFL thickness and optic nerve head parameters may be compared against the correlation with GCC. Also, the effect of check size on sensitivity of PERG in early glaucoma and OHT detection needs to be further studied. Follow up of OHT cases with abnormal PERG is needed to establish its ability to predict conversion to glaucoma because it is well known that not all OHT cases will convert to glaucoma. PERG can be affected by many other diseases affecting the macula and visual pathway, so such conditions were considered in our exclusion criteria. Also, PERG represents the summed activity of RGCs and cannot detect focal pathology seen in RNFL assessment. So we recommend using PERG in combination with other glaucoma investigations and not an alternative to them in order not to miss cases with focal RNFL defect.

CONCLUSIONS

PERG can detect the dysfunctional, but still live RGCs earlier than OCT in OHT cases, allowing the early start of treatment that can restore the ganglion cell function before irreversible damage occurs.

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