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ORIGINAL ARTICLE

Optic Disc and Retinal Nerve Fibre Layer Changes in Parkinson's Disease

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ABSTRACT

This study was conducted to assess optic nerve and peripapillary retinal nerve fibre layer (RNFL) changes in patients with idiopathic Parkinson's disease (PD) and its correlation with disease duration and severity. Optic nerve parameters and RNFL thickness were measured in 24 PD patients and 25 age–gender-matched controls by Heidelberg Retinal Tomography II (Heidelberg Engineering, Dossenheim, Germany). Patients with visual acuity below 20/25 were excluded. The mean RNFL in the temporal sector was significantly thinner in the study group than the control group ($p = 0.020$). Additionally, disease severity and duration negatively correlated with optic disc parameters in some sectors.

Keywords: Optic disc, parkinson's disease, retinal nerve fibre layer

INTRODUCTION

Idiopathic Parkinson's Disease (PD) is a common neurodegenerative disease characterised by loss of dopaminergic neurons, mainly in substantia nigra. A reduction of retinal dopamine concentration was also reported in PD.[1,2] Previously described visual findings associated with PD are reduced spatial contrast sensitivity, motion perception abnormalities, colour deficiency, and visual hallucinations.[3]

Recently, changes in the retinal nerve fibre layer (RNFL) and macular thickness have been documented in several studies with small sample size, and it has been proposed that this may be associated with loss of dopaminergic cells and eventually functional visual abnormalities in PD.[4–8]

In this study, we aimed to assess the optic disc and RNFL in Parkinson's patients with ''healthy eyes''. We, therefore, investigated optic disc rim area, rim volume and RNFL changes using retinal tomography in patients with PD without visual impairment.

MATERIALS AND METHODS

This prospective study was approved by Ethics Committee and adhered to the tenets of the Declaration of Helsinki. The study was conducted in the Department of Ophthalmology and the Department of Neurology at Pamukkale University. The participants were patients with PD and age- and gender-matched healthy subjects as the control group. All participants provided informed consent.

All patients and controls underwent detailed ophthalmic evaluation including best-corrected visual acuity; colour vision; intraocular pressure measurement; biomicroscopic anterior segment examination; and dilated posterior segment examination. Exclusion criteria were: defective colour vision; Snellen visual acuity below 20/25; history of glaucoma; intraocular surgery; optic neuropathy; diabetic retinopathy; high myopia (>4D); or other diseases which can affect optic nerve function or can prevent optic nerve imaging were excluded.

All PD patients evaluated at the PD clinic were invited to participate in this study by the neurologist.

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Eventually 42 PD patients accepted to be evaluated at the ophthalmology department. Of 42 patients, 18 patients were excluded due to having visual impairment, colour vision defects or co-existing ocular pathologies even if not affecting vision.

Each patient with PD underwent neurological examination on the same day and disease severity was scored based on cognitive disturbances, activities of daily living, motor features of PD.[9] They were also categorised according to existence of tremor and postural instability status.

Optic nerve images were taken from the participants with full pupil dilation in a dim room using Heidelberg Retinal Tomograph II (HRT-II, Heidelberg Engineering, Dossenheim, Germany). HRT is a confocal laser scanning system which creates a 3-D image of the optic nerve head and gives information about the optic nerve and the peripapillary RNFL. Stereometric parameters were calculated automatically by the software. The values obtained from the HRT-II scan for the study included optic disc rim area, rim volume, and RNFL thickness in temporal, superotemporal, inferotemporal, nasal, superonasal, and inferonasal sectors.

Statistical analysis was performed by SPSS statistical software (SPSS 11.0.0 for MS Windows; SPSS Inc., Chicago, IL). Descriptive statistics were expressed as mean ± SD. Independent samples test and Pearson's correlation were used for statistical analysis. A value of $p < 0.05$ was considered significant.

RESULTS

A total of 49 eyes of 49 subjects were enrolled in the study. Of 49 subjects, 24 had PD and 25 were healthy controls. The mean age of the patients were 62.3 ± 7.9 (range 47–73) and 60.3 ± 7.6 (range 49–73) in the PD and control groups, respectively. In the PD group, 15(62.5%) patients were male and 9(37.5%) were female, whereas in the control group 14(56%) subjects were male and 11(44%) were female. The differences in age and gender between the groups were not significant ($p = 0.371$ and 0.644, respectively).

In study group, the mean duration of PD was 4.6 ± 3.2 (2–12) years and the mean score for disease severity was 16.8 ± 9.0 (6–38); 12 (50%) patients had tremor and 8 (33.7%) had postural instability. All PD patients were on treatment including L-DOPA (five patients), dopamine agonist (five patients), combination of L-DOPA and dopamine agonist (six patients), L-DOPA, dopamine agonist and monoamine oxidase B inhibitor (three patients), L-DOPA and monoamine oxidase B inhibitor (two patients), L-DOPA and glutamate agonist (two patients) and monoamine oxidase B inhibitor and dopamine agonist (one patient).

Tables 1–3 present the mean and sectoral measurements of rim area, rim volume and RNFL in the study and control groups. The difference in rim area and rim volume was not significant between the study and control group (Tables 1 and 2). The mean RNFL in the temporal sector was likely to be thicker in the control group than the study group ($p = 0.020$, t-test).

In the study group, disease duration negatively correlated with rim area in temporal sector ($r = -0.440$, $p = 0.036$) and rim volume in temporal sector ($r = -0.450$, $p = 0.031$) after controlling for the effect of age. Disease severity negatively correlated with rim volume for the inferonasal sector ($r = -0.479$, $p = 0.018$). Age, having tremor or postural instability did not significantly correlate with any of the ocular parameters in patients with PD.

DISCUSSION

In our study, temporal RNFL thickness was significantly thinner in patients with PD than that in controls. Disease duration showed a negative correlation with rim area and volume in the temporal sector

TABLE 1 Comparison of optic disc rim area by retinal tomography between patients with PD and controls.

	Parkinson $n = 24$	Control $n = 25$	p Value
Rim area (average, mm^2)	1.76 ± 0.42	1.95 ± 0.81	0.298
Rim area temporal sector	0.28 ± 0.10	0.34 ± 0.24	0.296
Rim area superotemporal sector	0.21 ± 0.04	0.25 ± 0.11	0.149
Rim area inferotemporal sector	0.23 ± 0.08	0.26 ± 0.12	0.311
Rim area nasal sector	0.48 ± 0.11	0.52 ± 0.18	0.411
Rim area superonasal sector	0.25 ± 0.05	0.28 ± 0.10	0.180
Rim area inferonasal sector	0.26 ± 0.07	0.28 ± 0.09	0.451

TABLE 2 Comparison of optic disc rim volume by retinal tomography between patients with PD and controls.

	Parkinson $n = 24$	Control $n = 25$	p Value
Rim volume (average, mm^3)	0.42 ± 0.19	0.55 ± 0.37	0.162
Rim volume temporal sector	0.02 ± 0.01	0.04 ± 0.06	0.283
Rim volume superotemporal sector	0.05 ± 0.02	0.07 ± 0.05	0.190
Rim volume inferotemporal sector	0.05 ± 0.03	0.06 ± 0.06	0.421
Rim volume nasal sector	0.15 ± 0.05	0.16 ± 0.08	0.332
Rim volume superonasal sector	0.08 ± 0.04	0.09 ± 0.07	0.391
Rim volume inferonasal sector	0.08 ± 0.04	0.10 ± 0.07	0.191

whereas disease severity showed a negative correlation with rim volume in the inferonasal sector.

An association between RNFL thickness and PD was first proposed by Inzelberg et al.[4] They showed that the thickness in the inferior quadrant of peripapillary RNFL was significantly thinner in PD patients ($n = 10$) than controls using optical coherence tomography (OCT) but they did not show any correlation between RNFL thinning and disease duration. It is suggested that dopaminergic loss in the retina might alter visual processing by modifications of receptive field properties of ganglion cells and their axons which form the RNFL.[1,4] Reduced dopaminergic input to a group of ganglion cells might cause abnormal production of glutamate and atrophy of these selected fibres.[4]

Subsequently Yavas et al.,[5] reported lower mean RNFL thickness in patients with PD ($n = 44$) using HRT with the exception of the temporal and superotemporal sectors. Altıntas et al.[6] assessed the correlation between retinal findings and clinical severity in 17 patients with PD. They found that there was a reduction of RNFL thickness, macular volume and thickness in patients with PD. Those parameters did not correlate with the severity or duration of PD. Similarly, in our study, RNFL did not correlate with disease duration, however, rim area and volume in temporal sector showed a significant negative correlation with disease duration after adjustment for age.

Hajee et al.[7] reported that the inner retina was significantly thinner in patients with PD ($n = 24$) than in controls and suggested that PD should be considered in the differential diagnosis of RNFL thinning. On the contrary, Aaker et al.[8] stated that the peripapillary RNFL and inner retinal thickness were not significantly different between PD patients ($n = 9$) and controls but macular thickness in three of nine subfields was different from normal values.

Recently, the temporal RNFL was shown to be thinner on OCT in Parkinson's patients ($n = 43$) compared to controls, however, this finding did not correlate with clinical findings.[10] In another study, Moschos et al.[11] reported that the mean inferior and temporal RNFL thickness was significantly lower in Parkinson's patients ($n = 16$) without visual impairment when compared to a control group. Similarly, in this study, we found that the temporal RNFL was thinner in patients with PD than controls. The underlying mechanism leading to sectoral thinning of the RNFL is unclear. Loss of the temporal RNFL was documented in mitochondrial optic neuropathies such as Leber hereditary optic neuropathy or dominant optic atrophy; and a mitochondrial pattern has also been proposed for PD.[10,12,13] Temporal RNFL thinning was also reported in autosomal recessive cone-rod dystrophy, spinocerebellar ataxia type 1 and multiple sclerosis.[12,14,15] Other than a mitochondrial pattern, localised breakdown of oxidative defence mechanisms and sensitivity of the temporal RNFL to early damage and subclinical disease activity were also suggested.[12,15] More evidence is needed to understand the mechanism of sectoral thinning of the RNFL.

In conclusion, the novel finding in our study is that we found sectoral thinning of the RNFL in patients with PD with good vision compared to age- and gender-matched controls. This finding indicates that axonal degeneration exists in the eye before visual dysfunction becomes evident in patients with PD. In future studies the detection of early findings may be of importance because of advances in protective treatment modalities which may result in preservation of structure before the patient becomes symptomatic. Future studies would show whether retinal or optic disc imaging will have a place in the care of patients with PD on a routine basis.

TABLE 3 Comparison of RNFL thickness by retinal tomography between patients with PD and controls.

	Parkinson $n = 24$	Control $n = 25$	p Value
RNFL (average, mm)	0.20 ± 0.08	0.24 ± 0.07	0.108
RNFL temporal sector	0.07 ± 0.02	0.09 ± 0.02	0.020
RNFL superotemporal sector	0.24 ± 0.08	0.28 ± 0.06	0.061
RNFL inferotemporal sector	0.20 ± 0.11	0.26 ± 0.09	0.074
RNFL nasal sector	0.23 ± 0.10	0.28 ± 0.09	0.102
RNFL superonasal sector	0.30 ± 0.09	0.30 ± 0.12	0.886
RNFL inferonasal sector	0.29 ± 0.13	0.34 ± 0.12	0.248

***Declaration of Interest*:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.
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