Evaluation of Corneal Endothelium and Retinal Nerve Fiber Parameters in Patients with Unilateral Pseudoexfoliation

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ABSTRACT

Purpose: Evaluation of corneal endothelium and retinal nerve fiber values in patients with unilateral pseudoexfoliation (PEX).

Material and methods: The patients were retrospectively evaluated; 30 eyes of 30 patients with unilateral PEX were specified as group 1, the contralateral 30 eyes of the same 30 patients without PEX were designated as group 2, and 30 right eyes of sex and age-matched healthy subjects were evaluated as a controls group (group 3). The study group consisted of 30 participants in total.

Central corneal thickness (CCT), endothelial cell density (CD), coefficient of variation (CV) and hexagonality (HEX) parameters were analyzed, which were measured using specular microscopy. Retinal nerve fiber thickness of the superior (SRNFL), nasal (NRNFL), inferior (IRNFL) and temporal (TRNFL) quadrants and also ganglion cell inner plexiform layer thickness (GC-IPL) were measured using optical coherence tomography and analyzed.

Results: The mean age of study group was 64,66±7,04 years. In group 2, SRNFL, NRNFL and IRNFL were significantly higher than in group 1; no other parameters showed any significant difference. SRNFL, NRNFL, IRNFL and TRNFL values were significantly higher in group 3 than in group 1; no other parameters were significantly different. IRNFL and TRNFL values were significantly lower in group 2 compared with group 3, no other significant differences were found between these two groups.

Conclusions: In patients with PEX, there were no difference in corneal endothelial parameters when compared with the contra lateral eyes of same patients with no PEX and eyes of healthy controls, whereas thinning was observed in some quadrants in terms of RNFL thickness.

Keywords: Pseudoexfoliation, Specular microscopy, Retinal nerve fiber.

INTRODUCTION

Pseudoexfoliation (PEX) is an important ocular symptom of several systemic disorders. PEX is known to be the most frequent seen and well understood cause of open angle glaucoma.[1] PEX is diagnosed clinically and its pathology is characterized by the existence of grey-white fibrogranular PEX material in the anterior capsule of the lens and/or pupil border of the anterior segment of the eye.[2,3] PEX material can be seen unilaterally or bilaterally, although usually it is asymmetrical or unilateral. Even if the other eye doesn't seem like it is affected, it is very likely that subclinical PEX exists in that eye.[1] In light and electron microscopy, as well as immunohistochemical and biochemical studies, PEX material has been seen in the skin, extraocular muscle, heart, lungs, liver, kidney and meninges.[4,5]

In recent studies, notable changes were seen on the optic nerve head and in retinal nerve fibers in patients with various types of glaucoma.[6] Involvement of the corneal endothelium and Descemet's membrane occur although it is very difficult to see with a biomicroscope. Electron microscopy evidence of passive deposition and active local in situ production of PEX material from the aqueous humor have been shown.[7]

The aim of our study was to compare one eye with unilateral PEX accompanied by involvement of the retinal nerve fiber, ganglion cell inner plexiform layer thickness (GC-IPL) cell layer, and corneal endothelium without glaucoma with other eye of the patients, as well as with a single eye of healthy subjects.

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MATERIAL AND METHODS

Files of patients who previously presented to presented to Karabuk University hospital for routine eye examination were scanned. The diagnosis of PEX was made by seeing PEX material in the anterior lens capsule or pupil border after mydriasis with 5% Tropikamid (Tropamid, Bilim Ilac, Istanbul, Turkey). Patients with unilateral PEX were included in the study. The eye with PEX was specified as group 1, and the contralateral eyes of the same patients were evaluated as group 2, and the right eye of age and sex-matched healthy individuals were considered as group 3. Patients who and/or whose relatives have had glaucoma, vision field loss, used ocular medication and had undergone surgery were excluded. Corneal specular microscopy was performed using a Topcon SP-1P, Japan, and central corneal thickness (CCT), endothelial cell density (CD), coefficient of variation (CV), and hexagonality (HEX) parameters were analyzed. Retinal optical coherence tomography (OCT) was performed using a Cirrus HD spectral-domain OCT Carl Zeiss Meditec Cirrus HD spectral-domain OCT Carl Zeiss Meditec, Dublin, CA.

The study was approved by the local ethics committee of Karabuk University. For statistical analyses, the Statistical Package for the Social Sciences Ver. 22 software (SPSS, Inc., Chicago, Illinois) was used. Results are expressed as mean±standard deviation. In independent groups, numeric variables were analyzed using the independent samples t-test, and paired t-tests were used in dependent groups. The level of statistical significance was specified as <0.05.

RESULTS

Twelve patients were male and 18 were female in the study group(s). The mean age of the patients was 64.66±7.04years.

The following results were obtained for group 1; CCT 528.46±30.63 µm, CD 2692.60±302.44 cell/mm^2, CV 33.26±3.99, HEX 55.33±6.14, SRNFL 109.93±8.23 µm, NRNFL 63.93±15.50 µm, IRNFL 110.26±27.83 µm, TRNFL 59.73±7.54 µm, and GC-IPL 82.86±6.40 µm.

The following values were obtained for group 2; CCT 526.00±30.56µm, CD 2730.93±412.55 cell/mm^2, CV 34.00±4.34, HEX 54.26±4.64, SRNFL 118.53±15.65 µm, NRNFL 77.13±22.00 µm, IRNFL 119.40±16.02 µm, TRNFL 60.46±9.73 µm, and GC-IPL 83.86±7.70 µm.

The SRNFL, NRNFL, and IRNFL values of group 2 were significantly higher than in group 1, unlike the other parameters (p=0.012, p=0.045, p=0.016, respectively) (Table 1).

In group 3, the following results were obtained; CCT 539.83±30.94 µm, CD 2582.96±389.86 cell/mm^2, CV 32.20±4.51, HEX 54.56±9.12, SRNFL 123.93±21.55 µm, NRNFL 80.66±11.60 µm, IRNFL 136.36±21.30 µm, TRNFL 69.33±11.21 µm, and GC-IPL 85.13±9.82 µm. When compared with group 1, SRNFL, NRNFL, IRNFL, and TRNFL values were significantly higher than in group 3, unlike other parameters (p=0.002, p=0.0001, p=0.0001, p=0.0001, respectively) (Table 2). The IRNFL and TRNFL values of group 2 were significantly lower than in group 3; no other parameters showed any differences (p=0.001, p=0.002, respectively) (Table 3).

DISCUSSION

PEX syndrome consists of anincrement of extracellular matrix material production, a decrement of material resorption, or both.[2] PEX material can be detected in the

Table 1. *Comparison and statistical significance levels of Group 1 and Group 2 (dependent groups) parameters.*

GROUPS		N	Mean	Std. Deviation	P value
CCT	1	30	528.46	30.63	
	2	30	526	30.56	0.15
CD	1	30	2692.6	302.44	
	2	30	2730.93	412.55	0.307
CV	1	30	33.26	3.99	
	2	30	34	4.34	0.272
HEX	1	30	55.33	6.14	
	2	30	54.26	4.64	0.166
SRNFL	1	30	109.93	8.23	
	2	30	118.53	15.65	0.012
NRNFL	1	30	63.93	15.50	
	2	30	77.13	22.00	0.045
IRNFL	1	30	110.26	27.83	
	2	30	119.4	16.02	0.016
TRNFL	1	30	59.73	7.54	
	2	30	60.46	9.73	0,56
GANG	1	30	82.86	6.40	
	2	30	83.86	7.70	0.127

CCT: Central corneal thickness, **CD:** Endothelial cell density, **CV:** Coefficient of variation, **HEX:** Hexagonality, **SRNFL:** Superior retinal nerve fiber layer thickness, **NRNFL:** Nazal retinal nerve fiber layer thickness, **IRNFL:** Inferior retinal nerve fiber layer thickness, **TRNFL:** Temporal retinal nerve fiber layer thickness, **GANG:** Ganglion cell-inner plexiform layer thickness

Table 2. *Comparison and statistical significance levels of Group 1 and Group 3 (independent groups) parameters.*

GROUPS		N	Mean	Std. Deviation	P value
CCT	1	30	528.46	30.63	
	2	30	539.83	30.94	0.158
CD	1	30	2692.6	302.44	
	2	30	2582.96	389.86	0.229
CV	1	30	33.26	3.99	
	2	30	32.2	4.51	0.336
HEX	1	30	55.33	6.14	
	2	30	54.56	10.83	0.175
SRNFL	1	30	109.93	8.23	
	2	30	123.93	21.55	0.002
NRNFL	1	30	63.93	15.50	
	2	30	80.66	11.60	0.001
IRNFL	1	30	110.26	27.83	
	2	30	136.36	21.30	0.001
TRNFL	1	30	59.73	7.54	
	2	30	69.33	11.21	0.001
GANG	1	30	82.86	6.40	
	2	30	85.13	9.82	0.294

CCT: Central corneal thickness, **CD:** Endothelial cell density, **CV:** Coefficient of variation, **HEX:** Hexagonality, **SRNFL:** Superior retinal nerve fiber layer thickness, **NRNFL:** Nazal retinal nerve fiber layer thickness, **IRNFL:** Inferior retinal nerve fiber layer thickness, **TRNFL:** Temporal retinal nerve fiber layer thickness, **GANG:** Ganglion cell-inner plexiform layer thickness

Table 3. *Comparison and statistical significance levels of Group 2 and Group 3 (independent groups) parameters.*

GROUPS		N	Mean	Std. Deviation	P value
CCT	1	30	526	30.56	
	2	30	539.83	30.94	0.087
CD	1	30	2730.93	412.55	
	2	30	2582.96	389.86	0.159
CV	1	30	34	4.34	
	2	30	32.2	4.51	0.121
HEX	1	30	54.26	4.64	
	2	30	54.56	10.83	0.215
SRNFL	1	30	118.53	15.65	
	2	30	123.93	21.55	0.271
NRNFL	1	30	77.13	22.00	
	2	30	80.66	11.60	0.44
IRNFL	1	30	119.4	16.02	
	2	30	136.36	21.30	0.001
TRNFL	1	30	60.46	9.73	
	2	30	69.33	11.21	0.002
GANG	1	30	83.86	7.70	
	2	30	85.13	9.82	0.581

CCT: Central corneal thickness, **CD:** Endothelial cell density, **CV:** Coefficient of variation, **HEX:** Hexagonality, **SRNFL:** Superior retinal nerve fiber layer thickness, **NRNFL:** Nazal retinal nerve fiber layer thickness, **IRNFL:** Inferior retinal nerve fiber layer thickness, **TRNFL:** Temporal retinal nerve fiber layer thickness, **GANG:** Ganglion cell-inner plexiform layer thickness

anterior capsule of the lens, outside the iris, in the trabecular meshwork process of the zonular area of the ciliary body, anterior surface of the vitreous, conjunctiva, cornea, aqueous humor, posterior ciliary artery, veins of vortex, central retinal artery, optic nerve sheaths, septa of the orbital fat tissue, and in palpebra skin. Light and electron microscopic studies, as well as immunohistochemical and biochemical methods have also shown the existence of PEX material in the skin, extraocular muscles, heart, lungs, liver, kidney and meninges.[4,5,8,9]

PEX material can be detected in one single eye or in both eyes but is usually asymmetrical or unilateral. In unilateral cases, even if the other eye doesn't seem to be effected, subclinical PEX will exist in that other eye.[1] Clinically unilateral involvement usually leads to bilateral involvement and in nearly 50% of cases, bilaterality is reported 5-10 years after diagnosis. PEX prevalence of the other eye is 6.8% in 5 years and 16.8% in 10 years.[10] Patients with bilateral PEX are older and have higher glaucoma rates than patients with unilateral involvement.[11] Corneal endothelium and Descemet's membrane are also involved even if it is hard to be seen with biomicroscope. Thus, it can be suggested that patients who were accepted as unilateral are indeed asymmetrical, bilateral cases.[10] We did not perform ultrastructural studies; therefore we didn't observe similar alterations in the contralateral eye of patients with PEX in our study.

Studies have shown that risk of corneal endothelial decompensation increases even without glaucoma and/or elevated IOP in eyes with PEX.[7] In addition, if affected endothelial cells are damaged further during standard glaucoma or cataract surgery, decompensation can occur more easily.[7,12] In our study we observed no vulnerability of eyes with PEX, without PEX and eyes of healthy

individuals in terms of CCT, CD, CV and HEX parameters. We can say that corneal endothelium is not affected when our findings on specular microscopy are evaluated. Among the known predisposition factors for glaucoma, PEX has the highest risk ratio. PEX is a risk factor for glaucomatous and morphologic alterations in the optic nerve head, and glaucoma or ocular hypertension are detected during diagnosis in 20% of cases; glaucoma develops in approximately half of all cases during diagnosis or after diagnosis.[13] In 1987, Henry et al.[14] investigated the risk of increased intraocular pressure in 469 eyes of 347 patients and reported 5.3% risk in 5 years and 15.4% risk in 10 years. Konstas et al.[15] observed a 40% risk of intraocular pressure elevation or glaucoma in 10 years. Slagsvold[16] noted that the risk of glaucoma development in 102 patients with PEX was 2.9% in 5 years.

Examination of optic nerve head and RNFL with objective, reliable and highly reproductive methods is very important in the early diagnosis and follow-up of glaucoma. Hence, loss of the RNFL layer occurs prior to alterations of the optic nerve head and vision field loss.

Hammer et al.[17] compared unilateral PEX with the contralateral eye and showed typical PEX material in the iris, ciliary epithelium, and dilator muscle of the iris, as well as extracellular matrix accumulation in juxtacanalicular connective tissue of the trabecular meshwork and degenerative alterations in iris pigment epithelium and the dilator muscle in the eye with PEX, concluding that extracellular matrix accumulation in the juxtacanalicular tissue, which is a critical area was a factor that increased resistance to outflow.

Aygen et al.[18] investigated the correlation between optic nerve head alterations and vision field in PEX, concluding that PEX had early glaucomatous features and could be evaluated as early glaucoma with regard to the vision field index and retinal tomography in spite of normal intraocular pressure. There are studies showing that RNFL and GCC are affected in varying degrees in patients with PEX.[19,20]

In our study, SRNFL and IRNFL were thinned by about 9 µm and NRNFL by 14 µm in group 1 compared with group 2. RNFL measurements showed a loss of about 14 µm in the superior, 17 µm in the nasal, 26 µm in the inferior, and 10 µm in the temporal quadrants in group 1 compared with group 3. The inferior and temporal quadrants were about 17 µm and 9 µm in group 2 and group 3, respectively. We detected thinning of the SRNFL, NRNFL and IRNFL in the PEX-affected eyes of patients compared with their other eye. Also, thinning was found of nerve fiber layers of all quadrants (SRNFL, NRNFL, IRNFL, and TRNFL) in eyes with PEX compared with the healthy controls. In addition, thinning of the IRNFL and TRNFL were found in the unaffected eyes of patients with unilateral PEX when compared with the healthy controls.

As a result, in patients with unilateral PEX, corneal parameters and GC-IPL aren't affected, various levels of thinning occur in the RNFL, which we conclude can give raise to glaucoma or sensitivity in terms of retinal nerve diseases.

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