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Static and dynamic pupil characteristics in pseudoexfoliation syndrome and glaucoma

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Background: To compare the static and dynamic pupillometry measurements in patients with pseudoexfoliation syndrome (PES), patients with pseudoexfoliation glaucoma (PEG) and age-matched healthy subjects using an automatic quantitative pupillometry system.
Methods: This prospective, cross-sectional study consisted of 40 patients with PES, 30 patients with PEG and 43 control subjects. Static pupillometry measurements including scotopic pupil diameter, mesopic pupil diameter, low photopic pupil diameter, and high photopic pupil diameter were undertaken. Subsequently, dynamic pupillometry measurements including resting diameter, amplitude of pupil contraction, latency of pupil contraction, duration of pupil contraction, velocity of pupil contraction, latency of pupil dilation, duration of pupil dilation, and velocity of pupil dilation were undertaken. These measurements were compared between the groups.
Results: The scotopic, mesopic, and low photopic pupil diameter values were statistically significantly lower in patients with PES and PEG compared with controls ($p < 0.001$). However, these parameters were similar between the patients with PES and PEG ($p > 0.05$). The mean values of high photopic pupil diameter were similar within all groups ($p = 0.54$). The amplitude of pupil contraction values of the patients with PEG was statistically significantly lower than the patients with PES and the controls ($p < 0.05$). Patients with PES also had significantly lower amplitude of pupil contraction values compared with controls ($p < 0.001$). Additionally, the velocity of pupil contraction values was statistically significantly higher in control subjects when compared to the patients with PES and PEG ($p < 0.05$).
Conclusion: This study demonstrated that accumulation of pseudoexfoliative material can cause alterations in static and dynamic pupillary characteristics and the progression from PES to PEG may be associated with reduced amplitude of pupil contraction values.

Key words: dynamic pupillometry, pseudoexfoliation glaucoma, pseudoexfoliation syndrome, pupil diameter, static pupillometry

Pseudoexfoliation syndrome (PES) is a complex and age-related systemic disorder characterised by the progressive accumulation of abnormal extracellular pseudoexfoliative material in ocular tissues.[1] This accumulation could be detected in almost all the structures of the anterior ocular segment including ciliary body, iris, iridocorneal angle, lens capsule, zonules and cornea.[1,2] Detecting PES is important since it might be associated with a broad spectrum of ocular manifestations including increased intraocular pressure, cataract formation, zonular instability and phacodonesis, blood-aqueous barrier dysfunction and inflammation, keratopathy and also markedly increased intra-operative and post-operative complications such as insufficient mydriasis, posterior capsule rupture, intraocular lens subluxation, and posterior synechiae.[1–4] Furthermore, PES is considered to be the most common identifiable reason of open-angle glaucoma.[5] Pseudoexfoliation glaucoma (PEG) is a common cause of blindness worldwide and tends to be more progressive and serious compared to primary open-angle glaucoma.[5,6]

Glaucoma is an optic neuropathy characterised by progressive and chronic loss of retinal ganglion cells and their axons. Analysis of pupillary light reflex is one way to assess the integrity of afferent visual pathways and abnormalities in pupillary light reflex usually present as a relative afferent pupillary defect.[7,8] The relative afferent pupillary defect might be observed in the conditions of asymmetrical retinal or optic nerve diseases including glaucoma. Measurement of pupillary response via infrared pupillography was introduced by Lowenstein and Loewenfeld,[9] and the recent developments in automated pupillometry devices have enabled quantitative, objective, non-invasive, and repeatable measurements of pupil diameter in addition to the pupillary kinetics.[10,11] Various studies have shown that primary open-angle glaucoma is associated with impairments in pupillary responses by using automated pupillometry.[12–14] It is also well known that pupillary changes such as poor mydriasis, due to the iris infiltration and fibrosis, are associated with PES.

This study aimed to evaluate the static and dynamic pupillary measurements in patients with PES and PEG using an automatic quantitative pupillometry system, and to compare these data with those of age-matched healthy subjects.

Patients and methods

Participants

This prospective, cross-sectional study was performed at a tertiary referral ophthalmology clinic. All study procedures were in accordance with the tenets of the Declaration of Helsinki, and the study protocol was approved by the Ethics Committee of the Ankara Numune Training and Research Hospital. Written informed consent was taken from all study participants.

The study included healthy subjects as a control group and patients with PES and PEG. The patients with PEG were followed at the glaucoma department and were maintaining their target intraocular pressure values with their topical medication. The patients with PES and the age- and sex-matched control subjects were recruited from patients who applied to the outpatient clinic for ocular check-ups and routine refractive assessment. The data from the right eyes of all participants were analysed.

The diagnosis of PES was based on the presence of pseudoexfoliative material accumulation on the anterior lens surface or at the pupillary margin, pupillary ruff defects and transillumination defects of the pupillary ruff and iris sphincter. The existence of pseudoexfoliative material was reassessed after pupillary mydriasis. PEG was defined as presence of the anterior segment findings of PES accompanied by an intraocular pressure > 21 mmHg without treatment and associated glaucomatous findings.[15] Only the PEG patients with stage 1 (mean deviation ≤ −6 dB) or stage 2 (−6 to −12 dB) glaucoma according to the Hodapp-Parrish-Anderson grading scale were included in this study. Additionally, the PEG patients who used brimonide tartrate were not included since brimonide is associated with altered pupil size.[16] The patients with PES and the control subjects had an intraocular pressure less than 21 mmHg, an open chamber angle and a normal optic disc appearance (cup-to-disc ratio ≤ 0.4, no cup-to-disc asymmetry, a normal neuroretinal rim with no glaucomatous changes such as localised rim loss, no disc haemorrhage). These non-glaucomatous subjects were examined by a glaucoma specialist to exclude the possibility of glaucoma or ocular hypertension.

Participants with any of the following situations were excluded: strabismus, nystagmus, history of any ocular surgery or laser treatment, trauma or uveitis, patients under systemic or topical corticosteroid treatment, corneal disease, retinal disease, neurological or other disorders of the vision system, and hyperopia or myopia of more than −5.00 D, and astigmatism more than −3.00 D cylinder. Patients who had intraocular pressure greater than 21 mmHg were also excluded. Since smoking might be associated with changes in pupil size,[17,18] only non-smokers were included. Additionally, only the subjects who had not used drugs or consumed alcohol during the previous year, had no diagnosis of diabetes mellitus, had taken no systemic medications during the last three months, and had not used any anti-prostate drugs such as prazosin, terazosin, or tamsulosin, were included. Participants with any of the following conditions, which may affect pupillary motility, were also excluded: iris and/or pupil anomalies such as coloboma, anisocoria, synechia, and sphincter tear; topical medications that may affect iris mechanics such as tropicamide, cyclopentolate, pilocarpin, and narcotic-derived medications; and those who were not co-operative enough to undergo pupillometry examinations. To grade the lens opacities of the participants, the Lens Opacities Classification System III was used and the participants who had cataracts graded greater than two on this classification system were also excluded.

Ophthalmic assessment

All participants underwent a full ophthalmic assessment including best-corrected visual acuity using the Snellen chart, gonioscopy with a Goldman three-mirror lens, intraocular pressure measurement using a Goldmann applanation tonometer, slitlamp biomicroscopy, and dilated fundus examination. The refraction measurements were performed using the same automatic refractor-keratometer device (RF-K2 Full Auto Ref-Keratometer; Canon, Tokyo, Japan) for each participant. The spherical equivalent (spherical component +1/2 cylinder component) was used to calculate the refractive error. In addition, eye movements were evaluated in all aspects of view and the clinical swinging flashlight test was performed to determine the afferent pupillary defects.

Pupillometry

The same clinician performed pupillometry measurements using the same automatic quantitative pupillometry system (MonPack One, Vision Monitor System; Metrovision, Pérenchies, France). Before the pupillometry examination, no contact ocular examination and pupil dilatation were performed. Pupillometry measurements were taken at least three days after the pupil dilation. The quantitative pupillometry system was equipped with near infrared illumination and a high-resolution camera (880 nm), which allowed measurements to be taken from binocular pupils under complete darkness and to provide precise control of stimulation parameters. The stimulus was white, obtained from a full-field backlight combining red (632 nm), green (523 nm), and blue (465 nm) light-emitting diode sources. This system allowed the clinician to take both static and dynamic pupillometry measurements and to take accurate measurements of pupil size (accuracy = 0.1 mm).[10] Three consecutive measurements were taken for each participant and average values were calculated for data analysis. Additionally, the automatic-release mode of the device was used to minimise examiner-induced errors, and only high-quality images were included in the study. For minimising the impact of circadian variation on pupillary response,[19] the pupillometry measurements were taken between 10:00 and 12:00 hours and in the same environmental conditions. To control fixation stability during pupil recording, the subjects were required to fixate on a target in the centre of the test field while stimuli were presented. Pupil recordings were only used in the study analysis if eye movements were within five degrees of the central fixation axis of the optical system and the infrared camera plane. During the measurements the pupil contours of the subjects were outlined on the image by the device software. The proprietary analysis software of the device was used to conduct automatic static and dynamic pupillometry. This software automatically outlined the pupil contours of the participants on the images, ensuring that measurements were accurate and taken under controlled lighting conditions (Figure 1). Subsequently, the software analysed the temporal and average response to successive visual stimuli with automated quantification of the following parameters: latency and duration of contraction and dilatation (ms); initial, minimum, maximum, and mean pupil diameter (mm); amplitude of contraction (mm); and contraction and dilatation speed (velocity) of the pupil (mm/s) (Figure 1).

The static pupillometry measurements were taken under several illumination levels

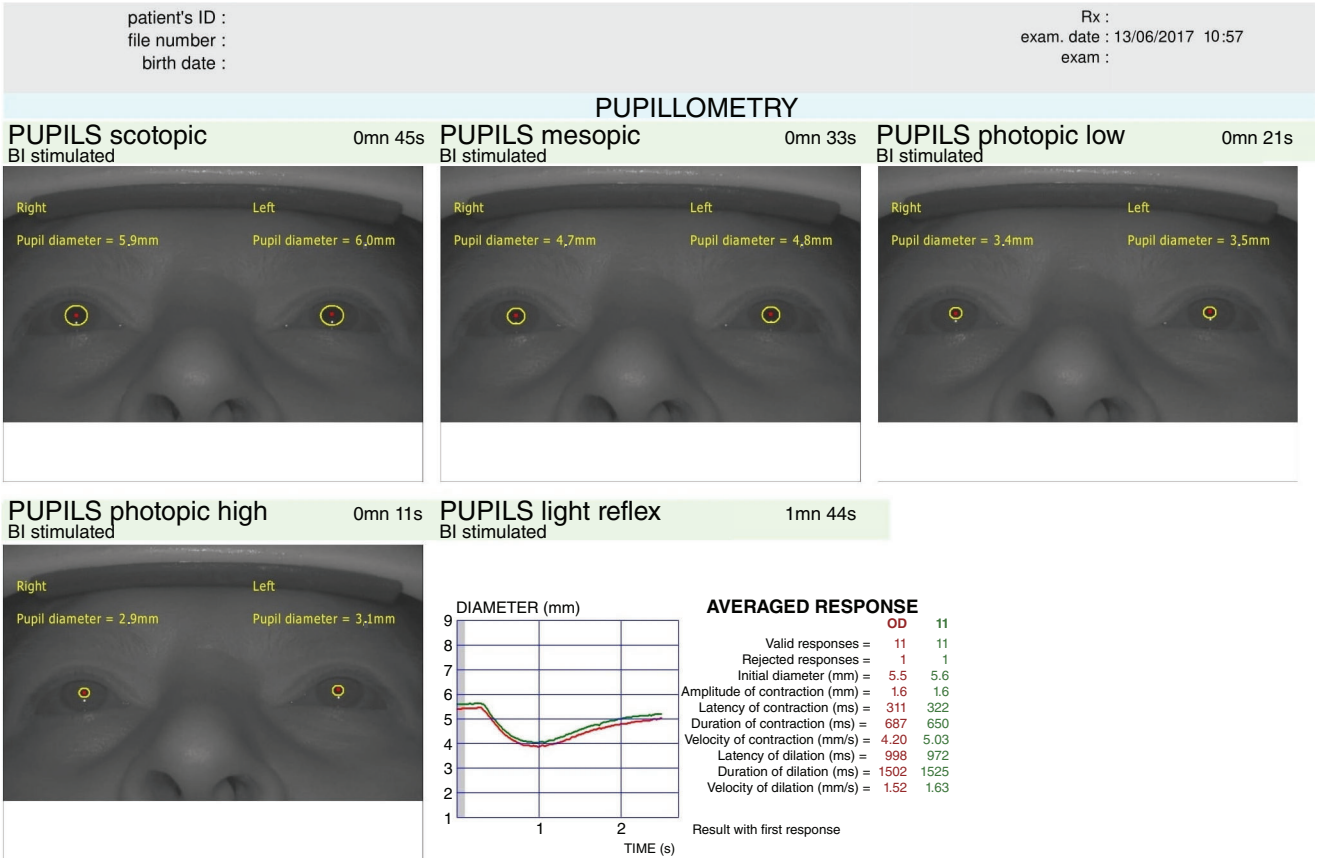

Figure 1. The output of static and dynamic pupillary characteristics via the automatic quantitative pupillary measurement system (Vision Monitor System; Metrovision, Pérenchies, France)

to measure pupil size in scotopic (0.1 cd/m^2), mesopic (1 cd/m^2), low photopic (10 cd/m^2), and high photopic (100 cd/m^2) vision conditions. Scotopic pupil diameter, mesopic pupil diameter, low photopic pupil diameter, and high photopic pupil diameter values were recorded (Figure 1). In darkness, after five minutes of darkness adaptation, dynamic pupillometry measurements were obtained for the duration of 90 seconds. Participants were examined using white light flashes (stimulation ON time 200 ms, stimulation OFF time 3,300 ms; total luminance 100 cd/m^2; total intensity 20 lux). The images of both eyes were acquired and processed in real time (30 images per second). The luminance output was measured using a Minolta LS100 luminance meter. The average response to successive visual stimuli (light flashes) was quantified using the following parameters: resting diameter, amplitude of pupil contraction, latency of pupil contraction, duration of pupil contraction, velocity of pupil contraction, latency of pupil dilation, duration of pupil dilation, and velocity of pupil dilation (Figure 1).

Statistical analysis

An a priori power analysis using the PASS 11 calculation software (Power and Sample Size, version 11) told us that we should enrol at least 30 participants from each group in the study. We enrolled 43 control subjects, 40 patients with PES and 30 patients with PEG. Accordingly, we found the power of our study to be 84.0 per cent. The study data were analysed using the Statistical Package for Social Sciences version 22.0 (IBM, Armonk, NY, USA). Descriptive statistics are presented as mean ± standard deviations, frequency distributions and percentages. Chi-squared test was used to analyse the categorical variables. Normal distribution of the variables was tested using visual (histogram and probability graphs) and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk tests). Equality of variances was checked by the Levene test. To determine whether there are any significant differences between the three groups, one-way analysis of variance (ANOVA) tests were used for normally distributed data, and Kruskal-Wallis tests were used for non-normally distributed data. Post hoc tests for pairwise comparisons were also performed. If ANOVA was used the independent sample t-tests were used for pairwise comparison and if Kruskal-Wallis was used the Mann–Whitney U-tests were used for pairwise comparison. A probability level of $p < 0.05$ was considered statistically significant.

Results

This study analysed 113 eyes of 113 participants. Of all participants, 43 subjects were in the control group, 40 patients were in the PES group and the remaining 30 were in the PEG group. The demographic data and

Details	Control (n = 43)	PES (n = 40)	PEG (n = 30)	p-value
Age, years, mean ± SD (range)	67.7 ± 5.9 (56 to 78)	67.1 ± 5.4 (54 to 78)	69.2 ± 6.7 (57 to 81)	0.101‡
Male/female, n/n	14/29	14/26	16/14	0.164†
BCVA, Snellen, mean ± SD (range)	0.85 ± 0.20 (0.6 to 1.0)	0.83 ± 0.18 (0.6 to 1.0)	0.79 ± 0.17 (0.5 to 1.0)	0.504‡
Refraction, SE, mean ± SD (range)	0.85 ± 1.40 (−2.00 to +2.00)	0.99 ± 1.40 (−2.50 to +2.25)	1.05 ± 1.66 (−1.50 to +2.75)	0.116‡
IOP, mmHg, mean ± SD (range)	15.1 ± 4.2 (9 to 20)	16.6 ± 3.4 (12 to 20)	14.8 ± 3.5 (11 to 19)	0.088‡

BCVA: best-corrected visual acuity, IOP: intraocular pressure, PEG: pseudoexfoliation glaucoma, PES: pseudoexfoliation syndrome, SD: standard deviation, SE: spherical equivalent.

†Chi-squared test.

‡Analysis of variance test (comparison among three groups).

Table 1. Demographic data and clinical characteristics of the groups

clinical characteristics of the groups are summarised in Table 1. Although the mean age in the PEG group was slightly older, there were no statistically significant differences between the groups with regard to age and gender ($p > 0.05$, for all; Table 1). The mean values of the best-corrected visual acuity, intraocular pressure, and refractive error were also similar between the groups ($p > 0.05$, for all; Table 1).

The static pupillometry measurements of the groups are shown in Table 2. The scotopic, mesopic, and low photopic pupil diameter values were statistically significantly lower in patients with PES and PEG compared with control subjects ($p < 0.001$, for all). However, these parameters were similar between the patients with PES and PEG ($p > 0.05$, for all). Moreover, the mean values of high photopic pupil diameter were similar within all groups ($p = 0.535$).

Table 3 demonstrates the dynamic pupillometry measurements of the groups. The patients with PES and PEG had statistically significantly lower resting pupil diameters when compared to controls ($p < 0.001$). The amplitude of pupil contraction values of the patients with PEG was statistically significantly lower than the patients with PES and the control subjects ($p < 0.05$). Additionally, the patients with PES also had significantly lower amplitude of pupil contraction values compared with controls ($p < 0.001$). Moreover, the velocity of pupil contraction values was statistically significantly higher in control subjects when compared to the patients with PES and PEG ($p < 0.05$). On the other hand, there were no statistically significant differences within all groups with regard to latency of pupil contraction, duration of pupil contraction, latency of pupil dilation, duration of pupil dilation and velocity of pupil dilation values ($p > 0.05$, for all; Table 3).

Discussion

Alterations in pupil size, shape, symmetry, response to light and response to near reflex can give clinicians a hint for the diagnosis of many neurological and ocular disorders and these alterations may also be related to history of medication, surgery or trauma.[20–22] However, subjective pupillary examination could be significantly affected from several factors such as ambient illumination, light stimulus intensity, and the clinicians' experience. Pupillometry devices can

Measurement	Control (n = 43) Mean ± SD (range)	PES (n = 40) Mean ± SD (range)	PEG (n = 30) Mean ± SD (range)	p-value
Scotopic PD, mm	5.44 ± 0.81 (4.20 to 7.30)	4.50 ± 0.90 (3.20 to 6.70)	4.39 ± 0.83 (3.20 to 6.60)	**< 0.001**[a†] **< 0.001**[b§], **< 0.001**[c§], 0.225[d§]
Mesopic PD, mm	4.50 ± 0.71 (3.30 to 6.30)	4.14 ± 0.60 (3.10 to 5.50)	4.07 ± 0.64 (3.10 to 5.70)	**< 0.001**[a†] **< 0.001**[b§], **< 0.001**[c§], 0.448[d§]
Low photopic PD, mm	3.52 ± 0.57 (2.30 to 4.80)	3.15 ± 0.13 (2.20 to 4.50)	3.13 ± 0.50 (2.30 to 4.50)	**< 0.001**[a†] **< 0.001**[b§], **< 0.001**[c§], 0.570[d§]
High photopic PD, mm	2.20 ± 0.60 (2.00 to 4.30)	2.16 ± 0.58 (1.90 to 4.10)	2.15 ± 0.55 (2.00 to 4.00)	0.535[a‡]

PD: pupil diameter, PEG: pseudoexfoliation glaucoma, PES: pseudoexfoliation syndrome, SD: standard deviation.

[a]Significance in analysis of variance (comparison among three groups).

[b]Significance between controls and PES (pairwise comparison).

[c]Significance between controls and PEG (pairwise comparison).

[d]Significance between PES and PEG (pairwise comparison).

Bold values indicate $p < 0.05$.

†Analysis of variance test (comparison among three groups).

‡Kruskal-Wallis test (comparison among three groups).

§Independent sample t-test (pairwise comparison).

Table 2. Static pupillometry measurements of the groups

Measurement	Control (n = 43) Mean ± SD (range)	PES (n = 40) Mean ± SD (range)	PEG (n = 30) Mean ± SD (range)	p-value
Resting diameter, mm	4.68 ± 0.85 (3.30 to 6.40)	4.28 ± 0.76 (3.20 to 6.00)	4.21 ± 0.73 (3.30 to 5.90)	**< 0.001**[a†] **< 0.001**[b], **< 0.001**[c], 0.311[d]
Amplitude of pupil contraction, mm	1.55 ± 0.41 (0.60 to 2.40)	1.15 ± 0.36 (0.60 to 1.70)	1.05 ± 0.33 (0.6 to 1.40)	**< 0.001**[a‡] **< 0.001**[b¶], **< 0.001**[c¶], **0.002**[d¶]
Latency of pupil contraction, ms	223 ± 75 (53 to 348)	250 ± 81 (55 to 369)	255 ± 85 (60 to 381)	0.095[a†]
Duration of pupil contraction, ms	648 ± 129 (120 to 956)	691 ± 199 (158 to 1,159)	703 ± 227 (154 to 1,427)	0.128[a†]
Velocity of pupil contraction, mm/s	5.19 ± 1.29 (2.27 to 10.06)	4.30 ± 1.48 (2.20 to 8.03)	3.96 ± 1.14 (1.77 to 6.58)	**< 0.001**[a†] **0.003**[b§], **< 0.001**[c§], 0.057[d§]
Latency of pupil dilation, mm/s	888 ± 106 (468 to 1,067)	914 ± 135 (506 to 1,373)	954 ± 192 (535 to 1,651)	0.196[a‡]
Duration of pupil dilation, ms	1,390 ± 197 (563 to 1,800)	1,500 ± 184 (702 to 1,870)	1,511 ± 177 (736 to 1,905)	0.073[a†]
Velocity of pupil dilation, mm/s	2.22 ± 1.62 (1.52 to 7.48)	2.05 ± 1.25 (1.40 to 6.31)	2.01 ± 1.28 (1.16 to 6.12)	0.213[a†]

PEG: pseudoexfoliation glaucoma, PES: pseudoexfoliation syndrome, SD: standard deviation.

[a]Significance in analysis of variance (comparison among three groups).

[b]Significance between controls and PES (pairwise comparison).

[c]Significance between controls and PEG (pairwise comparison).

[d]Significance between PES and PEG (pairwise comparison).

Bold values indicate $p < 0.05$.

[†]Analysis of variance test (comparison among three groups).

[‡]Kruskal-Wallis test (comparison among three groups).

[§]Independent sample t-test (pairwise comparison).

[¶]Mann–Whitney U-test (pairwise comparison).

Table 3. Dynamic pupillometry measurements of the groups

be used to obtain automatic, multiple, quantitative measurements of pupillary response to light under controlled, ambient lighting conditions. This improves the repeatability of the examinations, solves the problem of clinician-dependent errors and reduces false negative responses.[10,11,23]

Eyes with PES often have pupil abnormalities that are likely due to the progressive accumulation of pseudoexfoliative material in the iris. Additionally, eyes with PES usually show weak pupil dilation mainly because of the rigidity and fibrosis caused by iris sphincter muscle involvement. There are only limited studies evaluating the static and dynamic pupil characteristics of eyes with PES.[24–26] Ulviye et al.[24] assessed the pupil diameters of patients with PES in scotopic, mesopic, photopic and dynamic conditions and found that all investigated pupil measurements are statistically significantly lower in patients with PES compared to control subjects. These altered pupil sizes and dynamics were also observed even in the unaffected eyes of cases with clinically unilateral PES.[25,26]

The present study also demonstrated that the patients with PES and PEG have significantly lower scotopic, mesopic and low photopic pupil diameters and resting diameters compared to controls. On the other hand, these pupil diameters were similar between the PES and PEG groups. Park et al.[27] compared the pupil size in normal, glaucoma-suspect and glaucoma groups using Humphrey static perimetry and showed that mean pupil size tended to decrease significantly in glaucoma. They found there was no statistically significant difference in glaucoma suspects versus controls but the mean pupil size in the glaucoma group was statistically significantly smaller than in normal and glaucoma-suspect groups. However, our results showed that although all pupil sizes were shortest in the PEG group, there were no statistically significant differences in terms of pupil sizes between PES and PEG groups. This finding might be explained as follows. First, our study included patients with PES and PEG. It is well known these patients tend to have smaller pupil sizes. The accumulation of pseudoexfoliative material on the iris would affect both PES and PEG patients and for this reason, the differences in pupil size between PES and PEG subjects might not reach statistical significance. Second, we only included the PEG patients with stages 1 and 2 glaucoma. Because of the exclusion of late-staged glaucoma patients, the pupil sizes did not differ among the PES and PEG patients in our study. A recent study revealed that the comparison of pupil parameters between early and late glaucoma showed that the change in the pupil/iris ratio at minimum and maximum was significantly smaller in the late glaucoma group than in the early glaucoma group.[28] And lastly, we measured the pupil size with a pupillometry device not Humphrey static perimetry. Therefore, given the similarities of the PES and the PEG groups in most pupil measurements, and the exclusion of eyes with severe glaucoma, it is likely that the underlying aetiology is related to the accumulation of pseudoexfoliative material in the iris rather than due to underlying glaucomatous optic neuropathy.

A normal direct pupillary response to light reflects the integrity of the afferent and efferent arms of this part of the visuomotor system. Since glaucoma is a progressive optic neuropathy, asymmetrical disease can often lead to relative afferent pupillary defects.[7,8] Grozdanic et al.[29] observed that the rats with experimental elevated intraocular pressure suffer from pupillary light

reflex deficit which is correlated with degree of intraocular pressure elevation. Good correlation was also demonstrated between the degree of relative afferent pupillary defect and the inter-eye differences in mean deviation and estimated numbers of retinal ganglion cells which may suggested that pupillometry can be useful to quantify the asymmetric damage in glaucoma. Subsequently, the significance of pupillary light reflex evaluation in glaucoma, particularly in open-angle glaucoma, was more extensively investigated in human studies by using pupillometry devices. Kankipati et al.[12] examined the post-illumination pupillary response, which is driven by the intrinsically photosensitive retinal ganglion cells in patients with glaucoma, and demonstrated that the post-illumination pupillary response in patients with glaucoma is significantly decreased when compared to age-matched control subjects and the reduced post-illumination pupillary response is correlated with the severity of visual field loss. Feigl et al.[30] also showed that the patients with moderate and severe glaucoma have a dysfunctional intrinsically photosensitive retinal ganglion cells-mediated post-illumination pupillary response and the intrinsically photosensitive retinal ganglion cell function measured directly with the post-illumination pupillary response might become a clinical indicator of progressive changes in glaucoma. Further studies also investigated whether chromatic pupillometry could be used to detect impaired function of intrinsically photosensitive retinal ganglion cells in patients with primary open-angle glaucoma and whether the degree of pupillometric impairment correlates with optic nerve damage.[31,32] The results of these mentioned studies revealed that early stage of glaucoma is associated with reduced pupil responses to moderate and high irradiances of blue and red lights and also reduced pupillary responses to high-irradiance blue light are associated with greater visual field loss and optic disc cupping.[31,32] They also suggested that the short chromatic pupillometry test may be useful to detect glaucoma.[31,32] In another study, Martucci et al.[33] evaluated the pupillary light reflex in patients with different stages of open-angle glaucoma by a computerised pupillometry and showed a significant correlation between pupil contraction speed, minimum pupil diameter, percent pupil contraction, initial pupil diameter values and the stage of glaucoma. All of these aforementioned studies confirmed that glaucoma is associated with altered pupillary responses.

The results of this present study showed that the amplitude of pupil contraction and the velocity of pupil contraction measurements were statistically different in patients with PES and PEG compared to controls. On the other hand, the comparison of PES and PEG groups revealed that only the amplitude of pupil contraction values was significantly different between PEG and PES. We think that the accumulation of pseudoexfoliative material on the iris may affect pupil dynamics of patients with PES and PEG. Additionally, as the PES and PEG patients have smaller pupil sizes compared to controls, they might start from a lower diameter and thus had less room to come down, and thus the amplitudes were smaller in the PES and PEG groups. The differences between the PES and PEG subjects also may be related to the effect of glaucoma. Several studies also found that the peak pupil constriction amplitude was reduced in open-angle glaucoma.[31,33–35] However, the exact mechanisms responsible for these pupillary changes in glaucoma are not yet completely understood. Glaucoma is a progressive neurodegenerative disorder characterised by the apoptotic death of retinal ganglion cells triggered by different molecular pathways and is also involved in neuronal damage at the level of the afferent pathway and the central visual areas.[33,36] Additionally, recent studies discovered the intrinsically photosensitive retinal ganglion cells which express melanopsin and directly contribute to the post-illumination pupillary response.[37,38] Various studies exhibited that these intrinsically photosensitive retinal ganglion cells are damaged in glaucomatous eyes, suggesting the alterations in pupillary responses in glaucoma could be related to the loss of these intrinsically photosensitive retinal ganglion cells.[30–32]

This study had a number of limitations. First, it consisted of a relatively small number of participants, which can affect the validity of the results and their significance. Second, anti-glaucoma medications except brimonidine in the PEG group, might be a confounding factor effecting pupillary responses. On the other hand, Ba-Ali et al.[39] investigated the short-term effect of the anti-glaucoma drugs on the pupillary light reflex and post-illumination pupillary response and showed that dorzolamide reduces the pupil size, while timolol reduces both pupil size and maximal contraction to red light, but these effects are minute and not of clinical importance. Another limitation is that this study was performed cross-sectionally, so the generalisability of the findings may be limited.

To conclude, this study demonstrated that the accumulation of pseudoexfoliative material can cause alterations in static and dynamic pupillary characteristics and the progression from PES to PEG may be associated with reduced amplitude of pupil contraction values. Clinical implications of altered static and dynamic pupillary characteristics in PES and PEG warrant further comprehensive clinical studies.

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