Original Research Article

Assessment of pupil diameters in Pseudoexfoliation syndrome under scotopic, mesopic, photopic and dynamic conditions using infrared pupillometer

(Assessment of pupil diameters in Pseudoexfoliation syndrome)

Abstract

Aim: Our study aims to assess the mean pupil size under scotopic, mesopic, photopic and dynamic conditions in patients with PXS.

Methodology: This study was performed in Ophthalmology Clinic at İstanbul Bakırköy Dr.Sadi Konuk Training and Research Hospital. Fourty-six patients with PXS and 46 age and sex matched controls were included in the prospective study. The subjects were allowed at least 3 minute to adapt to the lighting condition in the room. Pupil diameters were measured with infrared (IR) pupillometer integrated within CSO Sirius Corneal Topographer (Costruzione Strumenti Oftalmici S.r.l,Italy) by the same examiner. The measurements were taken in scotopic, mesopic, photopic and dynamic conditions. Statistical analyses were evaluated.

Results: Mean pupil diameter were significantly lower in the PXS group than control group for all measurements. Scotopic and mesopic pupil size were significantly lower in the PXS group than control group (p=0.0001). Also photopic and dynamic pupil size were significantly lower in the PXS group than control group (p=0.014, p=0.013).

Conclusion: The results suggest that pupillary light response in patients with PXS significantly was affected not only in scotopic and mesopic conditions but also in photopic and dynamic conditions.

Key Words: dynamic; mesopic; photopic; pseudoexfoliation syndrome; pupil size; scotopic.

INTRODUCTION

Pseudoexfoliation syndrome (PXS) is a genetically determined, age-dependent generalized disorder of the elastic fiber system, characterized by excessive production and accumulation of an elastotic material within a multitude of intra- and extraocular tissues [1]. PXS is diagnosed by visualising the pseudoexfoliative material on the pupillary ruff and/or on the anterior lens capsule. In ultrastructural studies, pseudoexfoliative material has been shown to be accumulated within conjunctiva, iris, ciliary epithelium, and the dilator muscle of fellow eyes in unilateral or asymmetric PXS [2,3]. Early stage of the disease, it may be recognized on the basis of the lens surface in addition to poor pupillary dilation and pigment-related signs including pigment dispersion and peripupillary atrophy [4]. PXS is known to be associated with pupil abnormalities. This is particularly important in situations that require cataract surgery as well pupil dilation [3,4]..

Pupil size has influenced by various factors, such as the light stimulus and the stimulated eye, retinal illumination, accommodative state of the eye, sensory and emotional state, various neuro-psychiatric diseases, drugs, as well as the age and diabetes [5-8]. However, studies as regards dynamic muscle functions and pupil function with PXS are rare [9,10].

From this perspective, our study aims to assess the pupil size under scotopic, mesopic, photopic and dinamic conditions in patients with PXS.

MATERIAL AND METHODS

This prospective study was performed in Ophthalmology Clinic at İstanbul Bakırköy Dr.Sadi Konuk Training and Research Hospital. Fourty-six patients with PXS and 46 age and sex matched controls were included in the study. The research followed the tenets of the Declaration of Helsinki, with local ethical commitee approval and the full informed consent of patients. A complete routine ophthalmological examination was applied to all subjects. Retinal or optic pathologies and other ocular pathologies such as glaucoma, ocular surgeries and neuro-psychiatric diseases, the subjects with anterior segment and angle anomalies, diseases affecting the autoimmune system like diabetes, uveitis, pupil anomalies like posterior synechia, sleeplessness (including those with a history of partial sleeplessness) or with previous medical treatment like pilocarpin or other topical and oral medications that may affect autonomic function were excluded. The diagnosis of PXS were made by visualising the pseudoexfoliative material on the pupillary ruff and/or on the anterior lens capsule. Furthermore, the eyes with PXS were examined with Optical Coherence Tomography measurements in addition to the intraocular pressure to exclude glaucoma. In the study, it was included same eyes of patients with unilateral PXS, right eyes of patients with bilateral PXS and right eyes of control groups. In control group, unaffected eyes of patients with unilateral PXS were not included due to reasons such as pseudophakia, cataract, possible physiological anisocoria.

The subjects were allowed at least 3 minute to adapt to the lighting condition in the room. Pupil diameters were measured with infrared (IR) pupillometer integrated within CSO Sirius Corneal Topographer (Costruzione Strumenti Oftalmici S.r.l,Italy) by the same examiner without knowing their study groups. The CSO Sirius Corneal Topographer consists of a placido disc topographer, a 3 D rotating Scheimpflug camera, aberometer and integrated IR pupillometer. It was used binocular photomotor stimulus that both eyes perceive the same

illumination. Also IR pupillometer had characteristics of dinamic pupillometry. The measurements were applied in scotopic, mesopic, photopic and dynamic conditions. ***Scotopic***, in which the only visible light source is the LED source (0.4 lux). ***Mesopic,*** in which the disk is illuminated in such a manner as to bring ambient light intensity to about 4 lux. ***Photopic***, in which disk is illuminated in such a manner as to bring ambient light intensity to about 40 lux. Another type of lighting condition, called ***Dynamic,*** capture has begun with the rings disk fully illuminated (500 lux ca.); it was switched off at the moment capture begins. In this manner, it is possible to monitor pupil dilation. in conditions from photopic to absence of light (scotopic conditions) and analyze pupil size and pupil offset instant by instant.

Statistical Analysis

Statistical calculations were performed with (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) program for Windows. Besides, standard descriptive statistical calculations (mean and standard deviation), unpaired t test was used in the comparison of groups and Chi square test was performed during the evaluation qualitative data. *Pearson Correlation test used* to study the relationship between the variables. Statistical significance level was established at $p<0,05$.

RESULTS

In this study, it was included fourty-six patients with PXS and 46 sex, age-matched control subjects. There were no statistically significant differences in age and sex. The demographic data are listed in Table 1.

Pupil diameter in scotopic condition was measured between 2.65mm and 5.56 mm in PXS group, 3.65mm and 6.52mm in control group. It was mesured in mesopic condition

between 2.43mm and 5.35mm; 2.93mm and 6.44mm, in photopic condition between 2.09mm and 4.99mm; 2.47mm and 5.74mm and dynamic pupil diameter between 2.3mm and 4.67; 2.49mm and 5.07mm respectively. Mean pupil diameters were significantly lower in the PXS group than control group for all measurements. Scotopic and mesopic pupil size were significantly lower in the PXS group when we compared with control groups ($p=0.0001$). Also photopic and dinamic pupil size were significantly lower in the PXS group when comparing with control groups ($p=0.014$, $p=0.013$). Pupil size under scotopic, mesopic, photopic and dynamic conditions are listed in Table 2.

Correlation analysis revealed strong correlation of pupil diameters in scotopic, mesopic, photopic and dynamic conditions of both PXS and control groups (Table 3).

DISCUSSION

In our study, we aim to assess the pupil size under scotopic, mesopic, photopic and dinamic conditions in patients with PXS. To our knowledge, this will be the first study that evaluates the pupil measurements of patients with PXS using IR pupillometer integrated within CSO Sirius Corneal Topographer, since the Pub-Med search and other literature researches did not reveal any other similar papers.

Pupil size has affected by many factors such as illumination conditions, age, microvascular diseases like as diabetes mellitus, accomodation, fatigue, sensory and emotional status, and various drugs. Traditionally, pupil size has been evaluated with static pupillometers [11]. The recent technological developments in pupillometers, particularly incorporation of IR systems provide standardized intensity and duration of test light exposed, non-invazive, easy applicable, low inter-observer and intraobserver changes [12-14] . In our study, pupil size was measured with IR pupillometer integrated within CSO Sirius Corneal

Topographer. Characteristics of this pupillometer include binocularity, objectivity, standardized illumination and dynamic pupil function.

The majority of articles compared various pupillometers using different techniques and devices [12,14-25]. The digital pupillometers allow examination of the dynamic pupil function in addition to scotopic, mesopic and photopic measurements of pupil size and provide objective data using a computer software. In these devices, intensities of test illumination are well-defined. IR pupillometers are able to take monocular or binocular mesurements. The fellow eyes taken with monocular pupillometer are affected due to fluctuations in room illumination. In contrary, measurements taken with binocular pupillometer can be more advantageous because of most likely real-life conditions simulated [19,26].

All types of devices have been proved to give objective, standardized, reliable and repeatable data [14-16,19,22-25,27-31]. Schallenberg et al. compared Colvard, Procyon, and Neuroptics pupillometers for measuring pupil diameter under low ambient illumination. They indicate that monocular pupillometry either with the Neuroptics or Colvard pupillometer is at least as accurate as using the Procyon [14]. This result agrees with the studies of Kohnen et al. and Michel et al. [16,32]. Kohnen et al. stated that hand-held IR pupillometers with their simpler designs and portable features can also track the dynamic pupil process in an experienced hand. Furthermore, they concluded that the digital IR device shows less variation in scotopic pupil diameter and has better interrater repeatability than the hand-held IR devices [16]. Bootsma et al. noticed that digital binocular IR pupillometry is superior for obtaining standardized measurements of pupil size, because it is much more closer to real-life conditions [19]. Some features of Procyon and Sirius IR pupillometer are similar in terms of binocularity, objectivity, standardization of illumination and dynamic measuring [21]. Altan

et al. concluded that the tendency of smaller pupil size measurements with the Ocular Wavefront Analyzer might be due to the slightly higher ambiance illumination or an effect of accomodative miosis when subjects fixated on the a red light-emitting diode target in this device. Also it emphasizes that the larger pupil diameter found with the Sirius than with the Ocular Wavefront Analyzer and NeurOptics pupillometers may represent the different illumination levels used with each instrument together with relaxation of accommodation due to target fogging and software interpretation. It was reported that different measurements are related not only with illumination and accommodation but also with measurement algoritms or technique differences of instruments [25]. In our study, it was used binocular IR pupillometry.

It is known that mydriasis in eyes with PXS is restricted [2-4]. While making literature research, we did not find studies about investigating pupil measurements using IR pupillometer. Yulek et al. were used videonystagmography in asymmetric pseudoexfoliation patients. They were measured the percent of change in pupillary diameter in one second during the change in pupillary diameter during fixation to an accomodative target at 30 cm that is the accomodative response, during the light reaction, during the convergence-induced miosis, and finally during the divergence-induced mydriasis, both at fixed speed. They were declared that the difference between control group and pseudoexfoliative eyes of patient with PXS; between unaffected eyes and pseudoexfoliative eyes of patient with PXS was significant [10]. But they were unable to take measurements in different illumination conditions. Moreover, lack of normative data for responses of pupil to different illumination conditions can be interpreted as a limiting factor. Our study stands out with more numerous patients enrolled and a device with nomogram. It has shown significant variations in patients with PXS for 3 different light intensities and dynamic response. However, it was influenced dilation more than miosis.

In our study, it was determined that the eyes of PXS have smaller pupil diameters than control groups. The results suggest that pupillary light response in patients with PXS significantly deteriorate not only in scotopic and mesopic conditions but also in photopic and dynamic conditions as well. According to our findings, pseudoexfoliation material seems that dilator muscles affect more profound than the sphincter muscles. Recently, cataract surgery is refractive surgery at the same time and visual expectations of individuals are extremely high. Physicians should choose the multifocal IOL that best suits individual patients' desired outcomes, increasing patients' visual outcomes and satisfaction. Therefore, we highlighted that pupil size assessments under variable illumination conditions could be useful along with careful preoperative evaluation, particularly for patients with PXS who need better intermediate vision and refractive multifocal IOL.

As Schlötzer-Schrehardt et al. say: "The Puzzle Continues"[1]. Does the smaller pupil size provide a decrease in mean correction in patients with PXS? Are the abberations of eyes less in PXS patients? How much does PXS affect the pupil velocity? We will continue to look for answers to these questions.

CONCLUSION

The results suggest that pupillary light response in patients with PXS significantly was affected not only in scotopic and mesopic conditions both also in photopic and dynamic conditions. We believe that our study will be useful for further researches.

References

1. Schlötzer-Schrehardt U. Pseudoexfoliation Syndrome: The Puzzle Continues. *J Ophthalmic Vis Res.* 2012;7(3):187-189.

2. Hammer T, Schlötzer-Schrehardt U, Naumann GOH. Unilateral or asymmetric pseudoexfoliation syndrome? An ultrastructurel study. *Arch Ophthalmol*. 2001;119:1023-1031.

3. Prince AM, Sreeten BW, Ritch R, Dark AJ, Sperling M. Preclinical diagnosis of pseudoexfoliation syndrome. *Arch Ophthalmol*. 1987;105(8):1076-1082.

4. Scharfenberg E, Schlötzer-Schrehardt U. PEX syndrome: Clinical diagnosis and systemic manifestation. *Ophthalmologe*. 2012;109(10):952-961.

5. Schlosser K, Maschuw K, Kupietz E, Weyers P, Schneider R, Rothmund M, Hassan I, Bartsch DK. Call-associated acute fatigue in surgical residents-subjective perception or objective fact? A cross-sectional observational study to examine the influence of fatigue on surgical performance. *World J Surg*. 2012;36(10):2276-2287.

6. Bremner F, Smith S. Pupil findings in a consecutive series of 150 patients with generalised autonomic neuropathy. *J Neurol Neurosurg Psychiatry*. 2006;77(10):1163-1168.

7. Charman WN, Radhakrishnan H. Accommodation, pupil diameter and myopia. *Ophthal Physiol Opt.* 2009;29(1):72-79.

8. Subbaram MV, Bullimore MA. Visual acuity and the accuracy of the accommodative response. *Ophthal Physiol Opt.* 2002;22(4):312-318.

9. Suzuki R, Kurimoto S. Intraocular muscle function in pseudoexfoliation syndrome. *Ophthalmologica*. 1992;204(4):192-198.

10. Yulek F, Konukseven OO, Cakmak HB, Orhan N, Simsek S, Kutluhan A. Comparison of the pupillometry during videonystagmography in asymmetric pseudoexfoliation patients. *Curr Eye Res*. 2008;33(3):263-267.

11. Meeker M, Du R, Bachetti P, Privitera CM, Larson MD, Holland MC, Manley G. Pupil examination: Validity and clinical utility of an automated pupillometer. *J Neurosci Nursing.* 2005;37(1):34-37.

12. Rosen ES, Gore CL, Taylor D, Chitkara D, Howes F, Kowalewski E. Use of a digital infrared pupillometer to assess patient suitability for refractive surgery. *J Cataract Refract Surg.* 2002;28(8):1433-1438.

13. Kanellopoulos AJ, Asimellis G, Georgiadou S. Digital pupillometry and centroid shift changes after cataract surgery. *J Cataract Refract Surg.* 2015;41(2):408-414.

14. Schallenberg M, Bangre V, Steuhl KP, Kremmer S, Selbach JM. Comparison of the Colvard, Procyon, and Neuroptics pupillometers for measuring pupil diameter under low ambient illumination. *J Refract Surg*. 2010;26(2):134-143.

15. Schnitzler EM, Baumaister M, Kohnen T. Scotopic measurement of normal pupil: colvard versus video vision analyzer infrared pupillometer. *J Cataract Refract Surg*. 2000;26(6):859-866.

16. Kohnen T, Terzi E, Bühren J, Kohnen EM. Comparison of a digital and handheld infrared pupillometer for determining scotopic pupil diameter. *J Cataract Refract Surg*. 2003;29(1):112-117.

17. Chaidaroon W, Juwattanasomran W. Colvard pupillometer measurement of scotopic pupil diameter in emmetropes and myopes. *Jpn J Ophthalmol*. 2002;46(6):640-644.

18. Netto MV, Ambrosio R Jr, Wilson SE. Pupil size in refractive surgery candidates. *J Refract Surg.* 2004;20(4):337-342.

19. Bootsma S, Tahzib N, Eggink F, de Brabander J, Nuijts R. Comparison of two pupillometer in determining pupil size for refractive surgery. *Acta Ophthalmol Scand.* 2007;85(3):324-328.

20. Mantry S, Banejeree S, Naaro S, Shah S. Scotopic measurement of normal pupil size with the Colvard pupillometer and the Nidek autorefractor. *Cont Lens Anterior Eye.* 2005;28(2):53-56.

21. Taşkıran Çömez A, Kömür B, Eser İ. Assessment of pupil diameters of Emmetropes and myopes under photopic, mesopic and scotopic conditions, using the infrared pupillometer integrated within Schwind Sirius multifunctional diagnostic device. *Turkiye Klinikleri J Med Sci.* 2012;32(5):1226-1234.

22. Scheffel M, Kuehne C, Kohnen T. Comparison of monocular and binocular infrared pupillometers under mesopic lighting condition. *J Cataract Refract Surg.* 2010;36(4):625-630.

23. Brown SM, Bradley JC. Comparison of 2 monocular pupillometers and an autorefractor for measurement of the dark adapted pupil diameter. *J Cataract Refract Surg*. 2011;37(4):660-664.

24. Bradley JC, Cohn CD, Wu PW, Brown SM. Comparison of a monocular pupillometer and the pupillometry function of a binocular free-viewing autorefractor. *J Cataract Refract Surg.* 2011;37(7):1257-1262.

25. Altan C, Kaya V, Basarir B, Celik U, Azman E, Akar S, Demirok A, Yilmaz OF. Comparison of 3 pupillometers for determining scotopic pupil diameter. *Eur J Ophthalmol.* 2012;22(6):904-910.

26. Kurz S, Krummenauer F, Pfeiffer N, Dick HB. Monocular versus binocular pupillometry. *J Cataract Refract Surg.* 2004;30(12):2551-2556.

27. Smith GT. Repeatability of the Procyon P3000 pupillometer. *J Refract Surg.* 2011;27(1):11.

28. Nasser CK, Singer R, Barkana Y, Zadok D, Avni I, Goldich Y. Repeatability of the Sirius Imaging System and agreement with the Pentacam HR. *J Refract Surg.* 2012;228(7):493-497.

29. Ho LY, Harvey TM, Scherer J, Balasubramaniam M, Dhaliwal FS. Comparison of Rosenbaum pupillometry card using red and blue light to Colvard and Iowa pupillometers. *J Refract Surg.* 2010;26(7):498-504.

30. Wachler BS, Krueger RR. Agreement and repeatability of infrared pupillometry and the comparison method. *Ophthalmology*. 1999;106(2):319-323.

31. Gedik S,Koktekir BE, Bakbak B, Gonul S. Comparison of pupil diameter measurement with Lenstar LS 900 and OPD Scan II. Not interchangeable devices. *Saudi Med J.* 2012;33(11):1239-1240.

32. Michel AW, Kronberg BP, Narvaez J, Zimmerman G. Comparison of 2 multiple-measurement infrared pupillometers to determine scotopic pupil diameter. *J Cataract Refract Surg.* 2006;32(11):1926-1931.

Table 1.Demographic data of pseudoexfoliation syndrome and control groups

		Pseudoexfoliation syndrome group		Control group		P
Age		73.5±6.57		73.43±6.92		0.963
Sex	**Female**	22	47.83%	20	43.48%	
	Male	24	52.17%	26	56.52%	0.675

Table 2. Mean pupil size under scotopic, mesopic, photopic and dynamic conditions

Mean Pupil Diameter	Pseudoexfoliaton Syndrome group	Control group	P
Scotopic	4.16±0.65	4.77±0.66	**0.0001**

Mesopic	3.85±0.67	4.56±0.68	**0.0001**
Photopic	3.28±0.66	3.64±0.72	**0.014**
Dynamic	3.14±0.56	3.42±0.5	**0.013**

Table 3. Results of the correlation analysis of pupil diameters in scotopic, mesopic, photopic and dynamic conditions of both groups

Pseudoexfoliation Group		**Scotopic**	**Mesopic**	**Photopic**	**Dynamic**
	r		**0.882**	**0.837**	**0.76**
Scotopic	**p**		**0.0001**	**0.0001**	**0.0001**
	r	**0.882**		**0.85**	**0.812**
Mesopic	**p**	**0.0001**		**0.0001**	**0.0001**
	r	**0.837**	**0.85**		**0.905**
Photopic	**p**	**0.0001**	**0.0001**		**0.0001**
	r	**0.76**	**0.812**	**0.905**	
Dynamic	**p**	**0.0001**	**0.0001**	**0.0001**	

Control Group		**Scotopic**	**Mesopic**	**Photopic**	**Dynamic**
	r		**0.962**	**0.716**	**0.724**
Scotopic	**p**		**0.0001**	**0.0001**	**0.0001**
	r	**0.962**		**0.792**	**0.781**
Mesopic	**p**	**0.0001**		**0.0001**	**0.0001**
	r	**0.716**	**0.792**		**0.849**
Photopic	**p**	**0.0001**	**0.0001**		**0.0001**
	r	**0.724**	**0.781**	**0.849**	
Dynamic	**p**	**0.0001**	**0.0001**	**0.0001**	