

ORIGINAL ARTICLE

Medicine Science 2021;10(4):1263-7

Comparison of pupillometry measurements in myopic, emmetropic and hyperopic children

Alper Halil Bayat¹, Muhammed Mustafa Kurt², Cetin Akpolat³¹Istanbul Medipol University, Esenler Hospital, Department of Ophthalmology, Istanbul, Turkey²Samsun Gazi State Hospital, Department of Ophthalmology, Samsun, Turkey³Sisli Hamidiye Etfal Training and Research Hospital, Department of Ophthalmology, Istanbul, Turkey

Received 02 May 2021; Accepted 11 May 2021

Available online 26.09.2021 with doi: 10.5455/medscience.2021.04.136

Copyright@Author(s) - Available online at www.medicinescience.org

Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.



Abstract

To compare spherical and cylindrical equivalent, and pupillometry measurements between non-amblyopic myopic, emmetropic, and hyperopic children. The study was conducted prospectively and cross-sectionally in a single-centered eye clinic. Three non-amblyopic groups were included in the study: myopic (Myopia Group), emmetropic (Emmetropia Group), and hyperopic (Hyperopia Group) children. The groups were compared in terms of best-corrected visual acuity (BCVA), intraocular pressure (IOP), spherical equivalent (SE), and pupillometry measurements, including minimum dynamic pupillometry, maximum dynamic pupillometry, mesopic pupillometry, and photopic pupillometry. The correlation analysis was also performed between the measurements. We noted significant differences in mean SE values between the three groups and between the paired groups ($p < 0.001$ for all). Similar mean cylindrical equivalent values were observed between the three groups and between the paired groups ($p > 0.05$ for all). The hyperopia group had the lowest mean minimum dynamic pupillometry, maximum dynamic pupillometry, mesopic pupillometry, and photopic pupillometry values (1.97 ± 0.57 , 5.23 ± 0.51 , 4.96 ± 0.41 , and 3.30 ± 0.54 , respectively). We found significant differences in all pupillometry measurements between the three groups ($p < 0.05$ for all). However, similar results were obtained in all pupillometry measurements between the paired comparison of emmetropia and hyperopia groups ($p > 0.05$ for all). We also did not observe any correlation between the pupil diameter and age or gender ($p > 0.05$ for both). Our study might be unique regarding the comparison of pupillometry measurements in non-amblyopic children with refractive errors. Myopia in the pediatric population may have potential pupillometric effects when compared to emmetropia and hyperopia. This should be considered in terms of the clinical relevance of pediatric refractive examination under different illumination conditions.

Keywords: Pupillometry, myopia, emmetropia, hyperopia

Introduction

Emmetropia is a visual situation that defined as the location of the conjugate focus of the retina at infinity when the accommodation is relaxed; therefore, the retina locates in the plane of the second principal focus of the dioptric complex of the reduced eye. In emmetropia, an object at infinite is imaged on the retina without accommodation [1]. However, parallel rays cannot focus on the retina in ametropic conditions. Ametropia describes the appearance of a refractive error, properly myopia, hypermetropia, or astigmatism; thus, a separation from the emmetropia [2].

Assessment of the pupillary light reflex with pupillometry enables an objective evaluation of photoreceptor health in the optic nerve and retina. The afferent pathway to control pupil size arises from ganglion cells, rods, and cones [3-5]. Different light wavelengths affect different retinal cells and may cause different pupillary light response, which is defined as chromatic pupillometry [6,7].

Pupillometry measurements allow to detect and evaluate the severity of glaucoma, optic neuropathies, as well as diabetic retinopathy, macular degeneration, and retinal dystrophies [8-11]. In addition, media clarity, ocular biometry, and refractive error might affect pupil diameter diameter [12,13]. Assessing the effect of refractive error on the pupil size, especially in the pediatric population in whom the prevalence of refractive disorders such as myopia and hyperopia are greater, is important for a more precise evaluation of pupillometric outcomes. The rate of myopia is rising worldwide, with a prevalence of 14% to 50% in Europe and the United States, and up to 80% in some East Asian countries

*Corresponding Author: Cetin Akpolat, Sisli Hamidiye Etfal Training and Research Hospital, Department of Ophthalmology, Istanbul, Turkey
E-mail: akpolatcetin@yahoo.com

[14, 15]. The prevalence of hyperopia and astigmatism also rise especially with age [16].

Minute pupil diameter alterations may not be detectable in the routine ocular examination. The introduction of automated dynamic pupillometry tools has enabled quantitative and objective measurement of pupil size and kinetic pupil responses to different light stimuli. Dynamic pupillometry has been commonly used, properly for the assessment of autonomic dysfunctions [17, 18]. According to our literature review, no reports have been documented regarding pupillometry measurement comparison in a non-amblyopic pediatric population. This study aims to compare pupil diameters measured with dynamic pupillometry under mesopic and photopic conditions in non-amblyopic myopic, emmetropic, and hyperopic children.

Materials and Methods

The current prospectively and cross-sectionally designed study was carried out in a tertiary eye clinic from April 2020 to February 2021. The Institutional Review Board (Istanbul Medipol University, E-10840098-772.02.1289) approved the present study. Informed consent was obtained from all parents of the children before the measurements. The study was conducted according to the tenets of the Declaration of Helsinki.

Participants

A total of 140 children (5-18 years) were recruited in this study. The children were assessed in three groups. The first group (Myopia Group) included 47 right myopic eyes of 47 children, the second group (Emmetropia Group, +0.75 to -0.25 D)

included 45 right emmetropic eyes of 45 children, and the third group (Hyperopia Group) included 48 right hyperopic eyes of 48 children. All participants had a detailed ocular examination, including best-corrected visual acuity (BCVA, log MAR), cycloplegic refraction examination, strabismus assessment, slit-lamp anterior segment evaluation, dilated fundus assessment, intraocular pressure (IOP, mmHg), measurements of spherical equivalent (SE) and cylindrical equivalent (both in diopters, D), as well as the pupillometry measurements of minimum dynamic pupillometry, maximum dynamic pupillometry, mesopic pupillometry, and photopic pupillometry. IOP measurements were performed after the pupillometry measurements. Exclusion criteria were amblyopia, strabismus, high refractive errors (> -6 D myopia and $+4$ D hyperopia), >0.50 astigmatism, media opacity, history of the previous history of glaucoma, corneal or conjunctival disease, ocular inflammation disease (e.g., uveitis), retinal or choroidal disorder, and previous ocular surgery.

Pupillometry measurement protocol

The pupillometry measurements were performed by the same experienced technician using the Aladdin HW 3.0 model (Topcon Canada Inc., Topcon, Canada) within 0.5mm-10mm. The measurements were specified under dynamic, mesopic and photopic conditions (Figure 1). As it is known, every pupil is not the same and many pupils are eccentric or fluctuate from a circular shape at different dilation stages. Dynamic pupillometry function provides the clinician to observe the pupil moving in real-time on the screen and thus compare it with the corneal diameter. This advantage enables a consistent and repeatable way to best ascertain the pupil center.

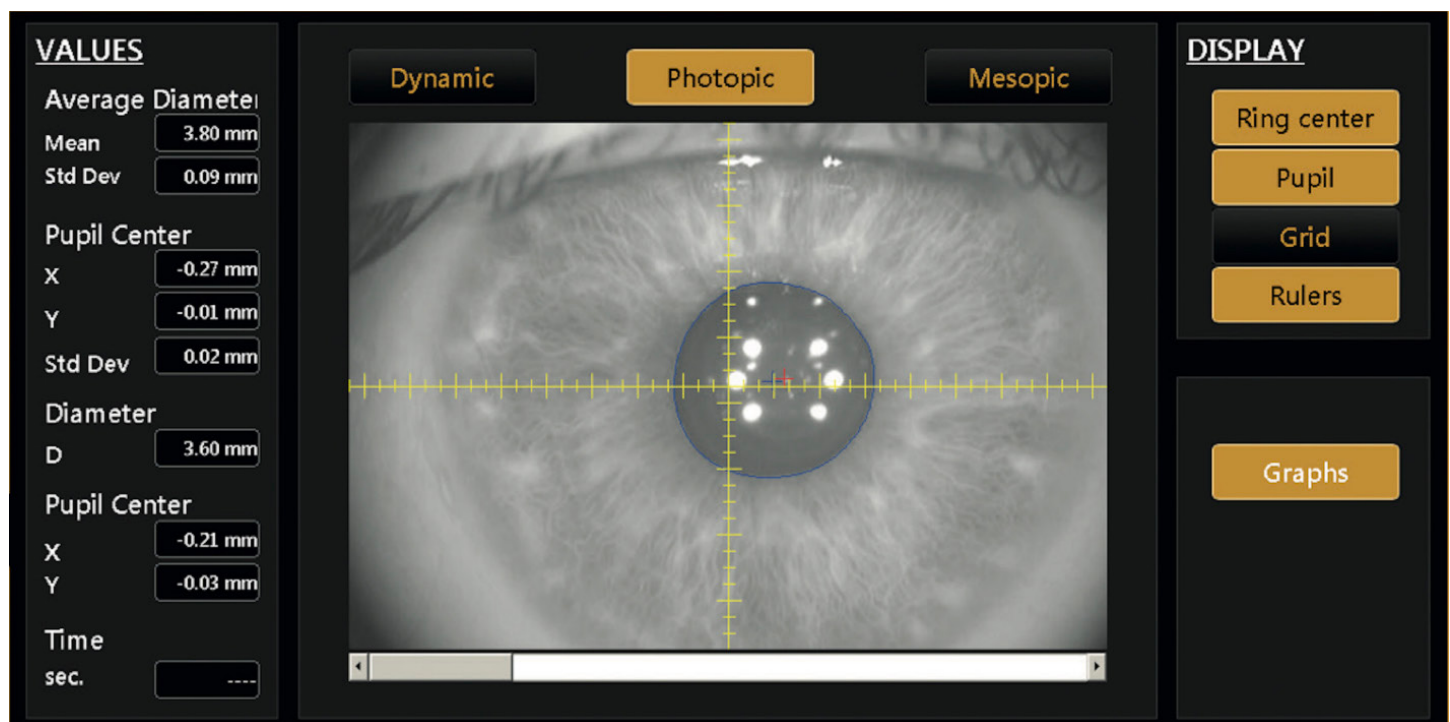


Figure 1. The Measurement of pupil diameter using the Aladdin HW 3.0 model (Topcon Canada Inc., Topcon, Canada)

Statistical analysis

The data was analyzed using SPSS 21.0 software (IBM Corp., Armonk, NY, USA). Constant parameters were described as the mean±standard deviation. We used the Shapiro–Wilk test to check normal distribution. Statistical analyses were performed by one-way ANOVA and independent samples t-tests. A Chi-square test was used for categorical analysis. Correlation analysis was performed with the Pearson correlation test. $P < 0.05$ was accepted as the significant point.

Results

Myopia, emmetropia, and hyperopia groups had similar mean age values of 14.86 ± 2.24 years, 14.93 ± 2.89 years, and 14.00 ± 2.26 years, respectively ($p = 0.650$). The myopia group included 25 female and 22 male children, the emmetropia group included 24 female and 21 male children, and the hyperopia group included 23 female and 25 male children ($p = 0.835$). We did not find significant correlations between pupil size and age or gender ($r = -0.256$ and $p = 0.138$, $r = 0.104$ and $p = 0.575$, respectively). Similar mean BCVA values were noted in myopia (0.036 ± 0.002 log MAR), emmetropia (0.022 ± 0.001 log MAR), and hyperopia (0.032 ± 0.002 log MAR) groups ($p = 0.742$). No significant IOP (intraocular pressure) values' differences were observed between myopia (13.88 ± 3.44 mmHg), emmetropia (14.02 ± 3.36 mmHg), and hyperopia (13.72 ± 4.08 mmHg) groups ($p = 0.656$).

The myopia group had a mean SE of -2.90 ± 1.22 D, the emmetropia group had a mean SE of -0.08 ± 0.34 D, and the hyperopia group had a mean SE of $+3.18 \pm 0.67$ D ($p < 0.001$). Regarding SE analysis, the significance levels between myopia and emmetropia groups, between myopia and hyperopia groups, and between the emmetropia and hyperopia groups were $p < 0.001$ for all comparisons. The myopia group had a mean cylindrical equivalent of -0.38 ± 0.27 D, the emmetropia group had a mean cylindrical equivalent of -0.35 ± 0.24 D, and the hyperopia group had a mean cylindrical equivalent of -0.31 ± 0.34 D ($p = 0.828$). Regarding cylindrical equivalent analysis, the significance levels between myopia and emmetropia groups, between myopia and hyperopia groups, and between the emmetropia and hyperopia groups were $p = 0.728$, $p = 0.574$, $p = 0.766$, respectively.

The pupillometry measurements were assessed in minimum dynamic, maximum dynamic, mesopic, and photopic conditions. We observed statistically significant differences in all these pupillometry measurements between the three groups ($p < 0.05$ for all). We also noted statistically significant differences in all these pupillometry measurements between myopia and emmetropia groups and between myopia and hyperopia groups ($p < 0.05$ for all). However, we did not find any statistically significant differences in any of these pupillometry measurements between the emmetropia and hyperopia groups ($p > 0.05$ for all) (Table 1).

Table 1. Comparison of pupillometry measurements between the myopic, emmetropic, and hyperopic children

	Myopia Group	Emmetropia Group	Hyperopia Group	p	p1	p2	p3
Minimum dynamic pupillometry	3.30 ± 0.59	2.39 ± 0.65	1.97 ± 0.57	< 0.001	< 0.001	< 0.001	0.152
Maximum dynamic pupillometry	6.78 ± 1.06	5.66 ± 0.98	5.23 ± 0.51	< 0.001	0.002	< 0.001	0.274
Mesopic pupillometry	6.04 ± 0.71	5.20 ± 0.90	4.96 ± 0.41	0.001	0.003	< 0.001	0.483
Photopic pupillometry	4.05 ± 0.75	3.43 ± 0.56	3.30 ± 0.54	0.003	0.002	0.026	0.614

p: One-way ANOVA analysis between the three groups, p1: Independent sample t-test analysis between myopia and emmetropia groups, p2: Independent sample t-test analysis between myopia and hyperopia groups, p3: Independent sample t-test analysis between the emmetropia and hyperopia groups

Discussion

The entrance pupil is the image of the real pupil that the examiner sees during the examination. Pupil diameter measurements used in clinical practices are also entrance pupil diameters. So, the pupil diameter measurements obtained in our study are the images of the entrance pupil. The entrance pupil is the virtual view of the real pupil created by the cornea. Indeed, the entrance pupil is placed nearly 0.5mm anterior to the real pupil and approximately 14% larger than the real pupil [19].

In the present study including non-amblyopic pediatric participants, we concluded that myopic children had a larger mean pupil size than the emmetropic and hyperopic children in dynamic, mesopic, and photopic pupillometry measurements. However, we did not note any significant difference in mean pupil diameter between the emmetropic and hyperopic children. We also did not observe significant correlations between pupil size and age or gender. The children in the three groups had similar mean BCVA and IOP values.

The measurement of pupil diameter and accurate definition of pupil size under various lighting circumstances is difficult and sophisticated. The major cause for this difficulty is that the pupil is dynamic and pupil diameter often alters even under the same lighting situations. Many reports have postulated that simple anisocoria and pupil disparity does exist and changes in individuals depending on accommodation and lighting [20]. The color of the iris, the condition of adaptation, the level of tiredness or attention, diurnal rhythms, medication, caffeine, and alcohol are among other factors that affect the pupil size [20, 21]. The pupillometry technique and the researcher performing the measurement also affect the measurement of pupil size [21]. So, several methods have been developed to overcome these conditions. The scotopic illumination is below 0.05 lux, and the photopic illumination is above 49 lux for the human eye [22]. The illumination ranges between these two values are described as mesopic illumination. The precise definition of pupil size in mesopic illumination is very important. Mesopic illumination is between photopic and scotopic illumination representing low, but not quite dark illumination conditions.

A study demonstrated that the association between spherical refractive error and pupil diameter was significant: Pupil diameter seemed to be inversely proportional to spherical refractive error, as the value of spherical refractive error raised, the pupil diameter reduced [23]. However, some studies reported no relation of pupil size with refractive error [24, 25]. Supporting our results, some reports concluded that pupil diameter was larger in myopic individuals than in the emmetropic and hypermetropic subjects [26-28]. This could be due to larger parameters of white-to-white measurement, axial length, and anterior chamber depth in myopic individuals [29]. Besides, the emmetropic and hyperopic subjects may require to accommodate more than uncorrected myopic individuals, thus the pupil will relatively constrict in emmetropia and hyperopia [30]. However, this relatively larger pupil size in myopia might be insignificant due to artifacts and the relaxation of accommodation by fogging the target light during the measurement (especially with wavefront aberrometer) [31]. Furthermore, some studies found an inverse association between pupil diameter and age, but no association between refractive error and gender [24,25, 32]. In contrast to these results, we found no relation between pupil size and age, which might be due to our specific selection of the pediatric population. Similar to these results, we did not note the relation between pupil size and gender. Despite some limitations including relatively small sample size and a lack of comparison with another measurement technique, our study may have a unique strength that compares the pupil size in non-amblyopic children with refractive errors and emmetropic refractive readings.

In conclusion, automated dynamic pupillometry can provide reliable and objective measurement of pupil size by enabling independent assessment of many parameters representing pupil actions. It is known that refractive error variations may influence pupil size. Suggesting this, our outcomes showed that using automated dynamic pupillometric measurements under mesopic and photopic conditions yielded larger mean pupil diameters in non-amblyopic myopic children, and no correlation was observed between the pupil size and age or gender. These results should be accounted for the clinical relevance of pediatric refractive assessment in case of various illumination conditions.

Conflict of interests

The authors declare that they have no competing interests.

Financial Disclosure

All authors declare no financial support.

Ethical approval

The Institutional Review Board (Istanbul Medipol University, E-10840098-772.02.1289) approved the present study.

References

- Hofstetter HW, Griffin JR, Berman MS, et al. Dictionary of visual sciences and related clinical terms. Boston, MA: Butterworth-Heinemann, 2000;p. 171.
- Hofstetter HW, Griffin JR, Berman MS, et al. Dictionary of visual sciences and related clinical terms. Butterworth-Heinemann. 2000:18.
- Merbs SL, Nathans J. Absorption spectra of human cone pigments. *Nature*. 1992;356:433-5.
- Hattar S, Lucas RJ, Mrosovsky N, et al. Melanopsin and rod-cone photoreceptive systems account for all major accessory visual functions in mice. *Nature*. 2003;424:76-81.
- Güler AD, Ecker JL, Lall GS, et al. Melanopsin cells are the principal conduits for rod-cone input to non-image-forming vision. *Nature*. 2008; 453:102-5.
- La Morgia C, Ross-Cisneros FN, Hannibal J, et al. Melanopsin-expressing retinal ganglion cells: implications for human diseases. *Vision Res*. 2011; 51:296-302.
- Rukmini AV, Milea D, Baskaran M, et al. Pupillary responses to high-irradiance blue light correlate with glaucoma severity. *Ophthalmology*. 2015;122:1777-85.
- Maynard ML, Zele AJ, Feigl B. Melanopsin-mediated post-illumination pupil response in early age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2015;56:6906-13.
- Tsika C, Crippa SV, Kawasaki A. Differential monocular vs. binocular pupil responses from melanopsin-based photoreception in patients with anterior ischemic optic neuropathy. *Sci Rep*. 2015;5:10780.
- Chibel R, Sher I, Ner DB, et al. Pupillometer for objective perimetry and diagnosis of patients with retinitis pigmentosa. *Ophthalmology*. 2016; 123:1898-911.
- Akpolat C, Kurt MM, Evliyaoglu F, et al. Pupil diameter study: Factors effecting pupil size in diabetic patients. *J Retina-Vitreous*. 2019;28:117-121.
- Abbott KS, Queener HM, Ostrin LA. The ipRGC-driven pupil response with light exposure, refractive error, and sleep. *Optom Vis Sci*. 2018; 95:323-31.
- Najjar RP, Sharma S, Atalay E, et al. Pupillary responses to full-field chromatic stimuli are reduced in patients with early-stage primary open-angle glaucoma. *Ophthalmology*. 2018;125:1362-71.
- Guillon M, Dumbleton K, Theodoratos P, et al. The Effects of age, refractive status, and luminance on pupil size. *Optom Vis Sci*. 2016;93:1093-100.
- Pan CW, Zheng YF, Anuar AR, et al. Prevalence of refractive errors in a multiethnic Asian population: the Singapore epidemiology of eye disease study. *Invest Ophthalmol Vis Sci*. 2013;54:2590-8.
- Yoo YC, Kim JM, Park KH, et al; Namil Study Group, Korean Glaucoma Society. Refractive errors in a rural Korean adult population: the Namil Study. *Eye (Lond)*. 2013;27:1368-75.
- Okutucu S, Civelekler M, Aparci M, et al. Computerized dynamic pupillometry indices mirrors the heart rate variability parameters. *Eur Rev Med Pharmacol Sci*. 2016;20:2099-105.
- Jackson KG, Malphrus EL, Blum E, et al. Pupillometric assessment of dysautonomia in pediatric bowel and bladder dysfunction: A pilot study. *J Pediatr Urol*. 2019;15:226.e1-226.e5.
- Uozato H, Guyton DL. Centering corneal surgical procedures. *Am J Ophthalmol*. 1987;103:264-75.
- Rukmini AV, Chew MC, Finkelstein MT, et al. Effects of low and moderate refractive errors on chromatic pupillometry. *Sci Rep*. 2019;9:4945.
- Pop M, Payette Y. Risk factors for night vision disturbances after LASIK for myopia. *Ophthalmology*. 2004;111:3-10.
- Rosen E. The pupil and refractive surgery. In: *Essential in Ophthalmology, Cataract and Refractive Surgery*. Verlag Berlin Heidelberg: Springer, 2005; pp. 289-302.
- Cakmak HB, Cagil N, Simavli H, et al. Refractive error may influence mesopic pupil size. *Curr Eye Res*. 2010;35:130-6.
- Winn B, Whitaker D, Elliott DB, et al. Factors affecting light-adapted pupil size in normal human subjects. *Invest Ophthalmol Vis Sci*. 1994;35:1132-7.
- Netto MV, Ambrósio R Jr, Wilson SE. Pupil size in refractive surgery candidates. *J Refract Surg*. 2004;20:337-42.
- Cakmak HB, Cagil N, Simavli H, et al. Corneal white-to-white distance and mesopic pupil diameter. *Int J Ophthalmol*. 2012;5:505-9.
- Bitirgen G, Daraghma M, Ozkagnici A. Evaluation of pupillary light reflex in amblyopic eyes using dynamic pupillometry. *Turk J Ophthalmol*. 2019 31;49:310-4.
- Yetkin E, Tekin K, Kiziltoprak H, et al. Evaluation of static and dynamic pupil characteristics in hyperopic anisometropic amblyopia. *Eur J Ophthalmol*. 2019;29:486-93.
- Yin G, Wang YX, Zheng ZY, et al; Beijing Eye Study Group. Ocular axial length and its associations in Chinese: the Beijing Eye Study. *PLoS One*. 2012;7:e43172.

30. Jones R. Do women and myopes have larger pupils? Invest Ophthalmol Vis Sci. 1990;31:1413-5.
31. Salmon TO, West RW, Gasser W, et al. Measurement of refractive errors in young myopes using the COAS Shack-Hartmann aberrometer. Optom Vis Sci. 2003;80:6-14.
32. Wilson MH, Edsell M, Imray C, et al. Birmingham Medical Research Expeditionary Society. Changes in pupil dynamics at high altitude—An observational study using a handheld pupillometer. High Alt Med Biol. 2008;9:319–25.