



ARAŞTIRMA / RESEARCH

Association between ocular biometric measurements and pediatric migraine

Oküler biyometrik ölçümler ile pediatrik migren arasında ilişki

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Abstract

Purpose: The aim of this study was to evaluate biometry parameters and anterior segment parameters in pediatric migraine patients compared to controls.

Materials and Methods: This prospective case-control study included 40 patients and 45 controls. All participants underwent a complete ophthalmological examination followed by measurement of anterior chamber depth (ACD), vitreous chamber depth (VCD), lens thickness (LT), axial length (AL), central corneal thickness (CCT), corneal volume (CV), anterior chamber volume (ACV), iridocorneal angle (ICA), pupil diameter (PD) and mean keratometry (K_m). Pupil diameter was compared between patients with and without photophobia. All evaluations were made in attack-free period. Pupil diameter was compared in migraine patients with and without photophobia. Intraocular pressure and biometry measurements were taken at the same time of day (10:00–12:00) in order to minimize the effects of diurnal variation. Right eye measurements were included in the study.

Results: The two groups showed no statistical differences in ACD, VCD, LT, AL, CCT, CV, ACV, ICA, PD, IOP, spherical equivalent or K_m . There was no difference in PD between patients with and without photophobia.

Conclusion: Pediatric migraine patients do not differ from controls in terms of biometry, corneal topography, or keratometry parameters. Studies with larger patient populations are needed to determine the relationship between ocular biometric parameters and migraine.

Keywords: Anterior segment, pediatric migraine, ocular biometry, pupil diameter

Öz

Amaç: Bu çalışmada pediatrik migren hastalarında biyometri ölçümlerinin ve ön segment parametrelerinin değerlendirilmesi ve sağlıklı çocuklarla karşılaştırılması amaçlanmıştır.

Gereç ve Yöntem: Bu prospektif vaka-kontrol çalışmasına yaş ve cinsiyeti uyumlu 40 pediatrik migren hastası ve 45 sağlıklı çocuk dahil edildi. Ölçümlerden önce tüm katılımcılar tam bir oftalmolojik muayeneden geçirildi. Ön kamara derinliği (ÖKD), vitreus uzunluğu (VU), lens kalınlığı (LK), aksiyel uzunluk (AU), merkezi kornea kalınlığı (MKK), kornea hacmi (KH), ön kamara hacmi (ÖKH), iridokorneal açısı (İKA), pupil çapı (PÇ) ve ortalama kornea kırıcılığı (K_m) değerlendirildi. Tüm değerlendirmeler ataksız dönemde yapıldı. Fotofobisi olan ve olmayan migrenli hastalarda pupil çapı karşılaştırıldı. Diüurnal varyasyondan en az oranda etkilenmek açısından göz içi basınç ölçümleri ve biyometri değerlendirmeleri günün aynı saatlerinde (10:00–12:00) yapıldı. Tüm katılımcıların sağ gözü çalışmaya dahil edildi.

Bulgular: Pediatrik migren grubuyla (27 kız, 13 erkek) kontrol grubu (30 kız, 15 erkek) arasında ÖKD, VU, LK, AU, MKK, KH, ÖKH, İKA, PÇ, göz içi basıncı, sferik eşdeğer ve K_m ölçümleri bakımından istatistiksel olarak anlamlı farklılık görülmedi. Migren grubu içerisinde fotofobisi olan hastalar ile olmayanların pupil çapları arasında anlamlı farklılık görülmedi.

Sonuç: Pediatrik migren hastalarında biyometri, korneal topografi ve keratometri ölçümlerinde sağlıklı çocuklara göre farklılık görülmemektedir. Pediatrik migren ile oküler biyometrik ölçümler arasındaki ilişkiyi incelemek için daha geniş hasta popülasyonlu çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Ön segment, pediatrik migren, oküler biyometri, pupil çapı

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INTRODUCTION

As in adults, headache is one of the most common complaints in the pediatric age group and one of the most common reasons for emergency admissions¹⁻⁶. Headache may originate from the central nervous system or may be seen as a symptom of other organ disorders^{1,4-6}. They are generally classified as primary headache disorders, such as migraines, and secondary headache disorders that occur due to an underlying condition. Migraine is common among children, adolescents, and adults worldwide. The severe symptoms of migraine can affect the quality of life of affected children in a similar way to childhood cancers, heart disease, and rheumatic diseases⁷. According to population-based studies, the prevalence of headache in the pediatric population is approximately 50% and the prevalence of migraine is 9.1%^{8,9}. The prevalence of episodic migraine is approximately 2-5% in preschool children, 10% in school-age children, and 20-30% in adolescent girls^{10,11}. Approximately 20% of the patients experience their first episode before the age of 5 years. Most patients have a family history of migraine^{12,13}.

Migraine is believed to have a polygenetic and multifactorial etiology¹⁴. There is still no single theory or hypothesis that adequately explains its pathogenesis. Although the vascular theory, which states that vascular dilatation causes attacks, has been invalidated by magnetic resonance angiography demonstrating an absence of arterial dilation, pediatric migraine studies have investigated optic nerve head, retinal nerve fiber layer (RNFL), ganglion cell complex (GCC), and choroidal thickness based on this theory¹⁵⁻¹⁷. In the study in which posteriorocular structure parameters were examined, 40 healthy controls and 40 pediatric migraine patients were compared. There was no statistically significant difference between the 2 groups for the average and sectoral values of total macula, ganglion cell layer, inner plexiform layer thickness. There was also no difference between the migraine and healthy groups for peripapillary RNFL thicknesses and subfoveal choroidal thickness¹⁶. In another study evaluating RNFL, optic nerve head, and macula, 24 pediatric migraine patients and 26 healthy controls were examined. Children with migraine showed significant variations in specific RNFL and optic disc parameters compared to control subjects¹⁷. To the best of our knowledge, although there are studies evaluating

selected biometric parameters in adults, no such study has been conducted in childhood migraine¹⁸. Koban et al assess the intraocular pressure and ocular biometric parameters in migraine patients during acute migraine attacks and compare them with painless period and healthy controls. In the migraine group, the average age was 34.5 years (± 11.19); in the control group, the average age was 30.1 years (± 14.15). There was not a statistically significant difference in intraocular pressure between the migraine patients during acute migraine attacks, painless period, and the controls. Also, the ocular biometric parameters did not significantly vary during the acute migraine attacks¹⁸. In this study, we aimed to compare anterior chamber depth (ACD), vitreous chamber depth (VCD), lens thickness (LT), axial length (AL), central corneal thickness (CCT), corneal volume (CV), anterior chamber volume (ACV), iridocorneal angle (ICA), pupil diameter (PD), intraocular pressure (IOP), mean keratometry (K_m), and spherical equivalent measurements in children with migraine and healthy children and to investigate the relationship between PD and migraine with visual aura (photophobia). All these parameters may be useful in evaluating the risk of developing diseases such as glaucoma and keratoconus in children with migraine, in the follow-up of refractive errors, and in calculating intraocular lens power.

MATERIALS AND METHODS

Study population

This prospective case-control study was approved by the Ethics Committee of Adana City Training and Research Hospital (10.03.2021 76/1309) and conducted in accordance with the rules of the Declaration of Helsinki. Informed consent forms were obtained from the parents or legal representatives of all participants.

The study included 40 children who were being followed up for migraine in the Adana City Training and Research Hospital Pediatric Neurology outpatient clinic and 45 healthy age- and sex-matched children who presented to the Adana City Training and Research Hospital Ophthalmology Clinic for routine check-up. Migraine was diagnosed according to the International Classification of Headache Disorders, 3rd edition (beta version) (ICHD-3-beta)¹⁹. Twelve of the 52 patients referred from the pediatric neurology clinic were excluded from the

study because they could not comply with the measurements. Duration of migraine, presence of aura, and family history were recorded. Participants between the ages of 8 and 18 years with refractive error less than 1 D and sufficient fixation and media clarity to obtain Pentacam images of adequate quality were included in the study. Those with any systemic disease other than migraine, amblyopia, glaucoma, corneal opacity, any history of ocular trauma or surgery, and those using contact lenses were excluded from the study.

Ocular examinations

All participants underwent visual acuity assessment by Snellen chart (Visual acuity was evaluated by converting to LogMAR), slit-lamp anterior segment and dilated fundus examinations, intraocular pressure measurements using Goldmann Applanation tonometry, keratometry, biometry, and corneal topography measurements. Intraocular pressure and biometer measurements were obtained at the same time of day (10:00-12:00) in order to minimize the effects of diurnal variation. For each instrument, all measurements were made by the same experienced technician. Assessments were performed while the patients were not having a migraine episode.

Refraction

Cycloplegic refraction was determined using an autorefractometer (Topcon RM-A2000; Topcon Medical Systems, Tokyo, Japan). Cyclopentolate hydrochloride 0.5% was instilled 3 times at 10 to 15 minute intervals before acquiring refraction measurements. Spherical equivalent was calculated by adding half of the cylindrical value to the spherical value.

Keratometry

An automated keratometer was used to perform keratometry (Topcon RM-A2000; Topcon Medical Systems, Tokyo, Japan). Mean keratometry readings were recorded.

Conventional A-scan ultrasonography

Axial length, ACD, VCD, and LT measurements were made using contact A-scan ultrasound (Aviso, Quantel Médical, Clermont-Ferrand, France). One drop of benoxinate 0.5% was instilled for topical anesthesia before measurement. Five measurements were made for each eye, and the mean values were obtained provided that the standard deviations did not exceed 0.1.

Scheimpflug imaging techniques

All participants' anterior segment parameters were evaluated using a Scheimpflug imaging system (Pentacam, Oculus Optikgerate, Wetzlar, Germany). Pentacam Scheimpflug imaging was performed in a dark environment to standardize measurements among all participants. Mydriatic drops were not administered before measurement. All scans were performed by the same technician, using automatic release mode to eliminate user-dependent variables. During measurement, the patient's head and chin are positioned properly and the patient is instructed to look at the blue fixation light. When the image has been focused and optimally adjusted, the device automatically starts the scanning process. To eliminate miscalculations due to low imaging quality, 3 measurements were made for each patient and a best quality measurement was selected. Central corneal thickness, CV, ACV, ICA, and PD values were measured in all participants. The participants' right eyes were included in the statistical evaluation.

Statistical analysis

The data were analyzed using SPSS version 21.0 software (IBM Corp, Armonk, NY). Shapiro-Wilk test was performed to check continuous variables for normal distribution. Comparisons between the migraine and control groups were performed using Student's t test for normally distributed variables and Mann-Whitney U test for non-normally distributed variables. Sex distribution was evaluated using chi-square test. Statistical significance level was accepted as ≤ 0.05 .

RESULTS

There were no significant differences in age or sex between the two groups ($p > 0.05$; Table 1). Girls accounted for 67.5% of the patient group and 66.7% of the control group. Snellen visual acuity was 0.00 logMAR in all participants in both groups. There were no statistically significant differences between the groups in IOP, spherical equivalent measurements, and K_m values ($p > 0.05$) (Table 2).

Twenty-one (53.8%) of the children in the migraine group had a family history of migraine. Mean disease duration was 18.45 ± 9.16 (6-36) months. Aura was present in 32.5% ($n = 15$) of the patients, while 27.5% ($n = 11$) had visual aura (photophobia). There were no statistically significant differences in ACD, VCD, LT, AL, CCT, CV, ACV, ICA, or PD values between

the two groups ($p > 0.05$) (Table 3). The mean PD was 3.46 ± 0.78 (2.14-5.04) mm among migraine patients with photophobia and 3.32 ± 0.59 (2.45-4.68) mm among those without photophobia ($p = 0.55$).

Table 1. Demographic data

	Migraine group	Control group	
	Mean \pm SD (min-max)	Mean \pm SD (min-max)	P_1
Age	12.95 \pm 2.93 (8-17)	12.42 \pm 3.03 (8-18)	0.42
	n (%)	n (%)	P_2
Sex			
Male	13 (32.5)	15 (33.3)	0.93
Female	27 (67.5)	30 (66.7)	

SD: Standard deviation; P_1 : Mann-Whitney U test; P_2 : Chi-squared test; min: minimum; max: maximum

Table 2. IOP, spherical equivalent, and keratometry measurements.

	Migraine group	Control group	
	Mean \pm SD (min-max)	Mean \pm SD (min-max)	P
IOP (mmHg)	13.53 \pm 1.65 (11-16)	13.33 \pm 1.67 (11-17)	0.51*
Spherical equivalent	0.0 \pm 0.03 (-1-0.25)	0.0 \pm 0.04 (-0.75-0.5)	0.99
K_m (D)	43.59 \pm 1.56 (39.75-47.88)	43.29 \pm 1.12 (41-45.88)	0.32

IOP: Intraocular pressure; K_m : Mean keratometry; SD: Standard deviation; P : Student's t test; *Mann-Whitney U test; min: minimum; max: maximum

Table 3. Biometry and topography parameters.

	Migraine group	Control group	
	Mean \pm SD (min-max)	Mean \pm SD (min-max)	P
ACD (mm)	3.59 \pm 0.3 (2.37-3.99)	3.66 \pm 0.32 (2.69-4.45)	0.54*
VCD (mm)	15.9 \pm 0.76 (13.78-17.74)	15.99 \pm 0.66 (14.34-17.49)	0.53
LT (mm)	3.64 \pm 0.19 (3.18-3.98)	3.66 \pm 0.26 (3.13-4.48)	0.73
AL (mm)	23.14 \pm 0.7 (21.16-25.13)	23.31 \pm 0.74 (21.25-24.98)	0.25
CCT (μ m)	548.85 \pm 32.16 (471-603)	544.38 \pm 37.83 (453-618)	0.56
CV (mm ³)	61.88 \pm 3.42 (54-68.2)	60.9 \pm 3.95 (51.1-69.3)	0.22
ACV (mm ³)	188.63 \pm 27.22 (143-240)	194.87 \pm 27.76 (112-264)	0.29
ICA ($^\circ$)	35.56 \pm 4.28 (26.3-45)	36.38 \pm 4.86 (24.6-46)	0.41
PD (mm)	3.36 \pm 0.64 (2.14-5.04)	3.22 \pm 0.56 (2.12-4.63)	0.27

ACD: Anterior chamber depth; VCD: Vitreous chamber depth; LT: Lens thickness; AL: Axial length; CCT: Central corneal thickness; CV: Corneal volume; ACV: Anterior chamber volume; ICA: Iridocorneal angle; PD: Pupil diameter; SD: Standard deviation; P : Student's t test; *Mann-Whitney U test; min: minimum; max: maximum

DISCUSSION

Despite numerous studies, it is still not possible to explain the pathogenesis of migraine with a single theory. The mechanisms underlying headache, aura, and photophobia remain unclear. The condition is

thought to be polygenetic and multifactorial, and the most widely accepted hypothesis today is the neuronal hyperexcitability. According to this theory, neuronal ion channel dysfunction leads to cortical spreading depression (CSD) and trigeminal system activation. Neurogenic inflammation of the

meningeal vessels causes migraine aura and headaches through central and peripheral trigeminal afferent activation^{1,4,6}.

In a study on ocular blood flow in migraine patients, central retinal artery and posterior ciliary artery resistance indices were reported to be higher in the pain-free period²⁰. Considering the contribution of changes in optic nerve head and retinal circulation to ganglion cell death, a previous study was conducted to evaluate RNFL, total GCL, IPL, and choroidal thickness in childhood migraine and revealed no significant differences from the control group¹⁶. In another study based on the vasogenic theory, there was no difference in ganglion cell layer (GCL) thickness compared to the control group, whereas differences were detected in some RNFL quadrants and some optical disc parameters such as disc area and cup volume¹⁷. Although a study evaluating IOP change and ocular biometric parameters in adult migraine patients has been conducted previously¹⁸. To the best of our knowledge, there are no studies evaluating ocular biometric parameters (ACD, VCD, LT, AL) and CCT, CV, ACV, ICA, and PD measured with Pentacam Scheimpflug imaging in pediatric migraine patients.

The anterior chamber lies between the posterior surface of the cornea in the front, the pupillary part of the lens and the anterior iris in the back, and the trabecular meshwork, scleral spur, ciliary body, and iris root at the periphery. The narrowest part of the anterior chamber is the ICA, which is the most important anatomical structure involved in drainage of aqueous humor from the anterior chamber. Gonioscopic examination is currently the gold standard for evaluation of the ICA, but methods such as Scheimpflug imaging are frequently used to assess anterior chamber parameters such as ICA and ACV because it is a noncontact method that provides more objective results and quantitative angle-related data.

Although ACD, VCD, LT, AL, ACV, and ICA were smaller in children with migraines in our study, the differences were not statistically significant ($p > 0.05$). Several studies have shown that changes in ciliary body and choroid thickness associated with choroidal perfusion may alter ACD due to movement of the iridolenticular diaphragm²¹. Although LT was smaller, reduction in ACD and ACV due to anterior shift of the iridolenticular diaphragm may have narrowed the ICA, leading to a mild increase in IOP, albeit statistically nonsignificant ($p = 0.51$). In addition, the anterior movement of the iridolenticular

diaphragm may have caused a higher PD in the migraine group, although it was not statistically significant ($p = 0.27$).

In our study, there was no significant difference between the groups in terms of CCT ($p > 0.05$). In previous studies investigating the relationship between migraine and dry eye, it has been claimed that dry eye is associated with decreased CCT²². Another study reported that dry eye may occur in migraine patients with high attack frequency and long disease duration²³. Therefore, patients with chronic migraine may be more likely to have dry eye and consequently reduced CCT. In a study of adult migraine patients, no difference was found in CCT measurements, consistent with our findings¹⁸. This was attributed to the patients' low attack frequency and short disease duration. Similarly, a difference in CCT may not have been observed in our study due to the patients' young ages and the short disease duration.

Previous studies have reported that CV decreases with age and in normal individuals shows a gradual increase from the center to the periphery^{24,25}. In our study, there was no significant difference in CV or K_m between the two groups, which were matched for age and sex ($p > 0.05$).

Migraine can occur with aura (visual, sensory, speech and/or language, motor, brainstem, and retinal auras) or without aura. Aura is reported by only 10-20% of children with migraine, usually occurring for the first time after the age of 8 years²⁶. Although it is not difficult to recognize migraine aura in adults, it can be difficult in children. The aura phase may precede the headache but more often occurs during the headache²⁶. Aura is frequently visual, but may also be sensory, motor, language, retinal, or brainstem related²⁶. The main distinguishing symptom between migraine and other headache disorders is photophobia, which is generally associated with phonophobia²⁷. The migraine group in our study included children over 8 years of age, of whom 32.5% ($n = 15$) had aura and 27.5% ($n = 11$) had visual aura (photophobia). Our proportion of patients with aura was higher than in the aforementioned studies. In an adult migraine study, PD measurements obtained from migraine patients during attacks and while asymptomatic were compared with a control group and no significant difference was observed¹⁸. Similarly, we also detected no significant difference in PD between the migraine and control groups in our study ($p = 0.27$). In addition, comparison of PD

between patients with and without visual aura (photophobia) revealed no significant difference ($p = 0.55$). However, PD tended to be larger in the migraine group than in the control group and in migraine patients with photophobia than those without. It has been previously reported that autonomic nervous system dysfunction in migraine, even if subclinical, may lead to pupillary abnormality²⁸. Among our findings, we can attribute the slightly higher PD in the visual aura group to the fact that we obtained measurements while the patients were asymptomatic, whereas aura usually accompanies migraine attacks. Moreover, although it was not statistically significant, the slight increase in PD in children with migraines may be associated with the subclinical effect of migraine on the autonomic nervous system.

In some studies, researchers' findings suggest an association between migraine and the risk of primary open angle glaucoma (POAG)²⁹. However, to date, no mechanisms have been described that could support the idea that migraine may increase the risk of progression of POAG²⁹. Therefore, comparing anterior segment and biometric parameters in pediatric migraine patients with healthy controls will shed light on further studies that will examine the relationship between migraine and POAG.

Our study had certain limitations. Firstly, because it would be unethical to subject pediatric patients to these examinations during an acute migraine episode, patients were not examined during an attack. Data obtained during an attack could have yielded different results. In addition, the effect of the frequency, severity, and duration of attacks on the studied parameters was not evaluated.

In conclusion, the results of this study indicated that ocular biometric parameters, anterior segment parameters measured with Pentacam Scheimpflug imaging, IOP, K_m , and spherical equivalents did not differ significantly in children with migraine compared to healthy controls and PD was not associated with visual aura. These data are helpful in understanding the pathogenesis of pediatric migraine, relationship between migraine and ocular biometric measurements and guiding future studies with larger patient samples.

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