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Original Article

Evaluation of retinal nerve fibre layer and ganglion cell complex thickness with optical coherence tomography in migraine patients

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Abstract

Aim: In this study, we aimed to assess thicknesses of retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) in patients with episodic migraine and to compare data between from patients with migraine and healthy individuals.

Material and Methods: The study included 44 eyes (right) of 44 patients with migraine who presented to neurology outpatient clinic and 54 eyes (right) of healthy individuals. In patients with migraine (with identified subtypes), demographic and clinical characteristics, Visual Analog Scale (VAS) and Migraine Disability Assessment Scale (MIDAS) results were recorded. After detailed ophthalmological examination, RNFL and GCC thicknesses were measured with optical coherence tomography (OCT) (Carl Zeiss Meditec AG, Jena, Germany, software version: 6.5.0.773). The values obtained were compared between groups. The correlation between VAS and MIDAS scores and RNFL and GCC thicknesses were assessed.

Results: Mean age was 36.05±8.84 years in migraine group and 32.89±10.89 years in control group. Mean time of follow-up was 5.50±3.42 years in patients with migraine. No significant differences were detected in mean RFNL and GCC thicknesses from all quadrants ($p>0.05$ for all). It was found that VAS and MIDAS scores were negatively correlated to mean RNFL thicknesses in temporal and inferior quadrants ($p<0.05$).

Conclusion: In our study, it was found that migraine did not affect in ocular structures of posterior segment such as RNFL and GCC thickness.

Keywords: Migraine; retinal nerve fiber layer; ganglion cell complex; optical coherence tomography.

INTRODUCTION

Migraine is a primary, episodic headache disorder accompanied by neurological, gastrointestinal and autonomic changes. Transient neurological symptoms (visual, motor or somatosensory) known as aura which may last a few hours to days can be seen in up to 30% of migraine patients (1). Thus, clinically, migraine is classified into two subtype: migraine without aura (MwoA) and migraine with aura (MwA) (2).

In the migraine pathogenesis, the most important mechanism is neurovascular system. Several studies have shown that vascular changes ocur in the ocular system during the attacks of migraine. It has been shown that cerebral blood flow in the occipital hemisphere diminishes during the attacks. This vasospasm can lead to chronic damage in the optic nerve head, retina, and eventually leading to ganglion cell death, which is inevitably reflected on retinal nerve fiber layer (RNFL) thickness. Retinal infarcts due to retinal artery occlusion have also been reported (3,4).

In recent years, optical coherence tomography (OCT) is being used for several neuro-ophthalmological procedures. OCT is a non-invasive, contact-free, reliable and reproducible imaging modality that uses 820 nm ultraviolet wavelength (5-7).

In the present study, we aimed to assess thicknesses of retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) in patients with episodic migraine and to compare data between from patients with migraine and healthy individuals.

MATERIAL and METHODS

The study included 44 eyes (right) of 44 patients who presented to neurology outpatient clinic and diagnosed

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as migraine based on International Headache Society (IHS) criteria and 54 eyes (right) of healthy individuals (2). The study was conducted in accordance to Declaration of Helsinki. Local Ethics Committee approved it. All participants gave written informed consent.

In all patients, age and frequency, duration and severity of attacks were recorded. The severity of headache was assessed by VAS (1, minimum pain; 10, most severe pain) [8]. The patients were asked to complete MIDAS test in order to determine disability rate. MIDAS test includes five items about school, workplace and home. MIDAS score is calculated based on number of miss work or school or productivity at work or school reduced by at least 50%. The patients are classified into 4 groups based on MIDAS score: group I, no or little disability (0-5 days); group II, mild disability (6-10 days); group III, moderate disability (11-20 days); group 4, severe disability (>21 days) (9-11).

All patients underwent detailed ophthalmological examination. Then, OCT imaging was performed by an experienced operator using Zeiss-Cirrus HD OCT (Carl Zeiss Meditec, AG, Jena, Germany, software version: 6.5.0.772), when image quality ≥7 was achieved. The RNFL thickness was measured across circle centered to optic nerve head (optic disc cube; 200x200; mean, superior, outer, inferior and inner quadrant RNFL) while GCC thickness was measured across circle centered fovea (macular cube, 512x128; superior and inferior GCC).

Exclusion criteria included patients with myopia, amblyopia, glaucoma, history of ocular surgery ,comorbid systemic disorders such as coronary artery disease, hypertension and diabetes mellitus, patients who had been diagnosed with Multiple Sclerosis, Parkinson's disease, or Alzheimer's disease.

Statistical analysis

All statistical analyses were performed by SPSS for Windows version 21.0. Continuous variables are summarized as mean ± standard deviation while qualitative variables are summarized as count and percent. Kolmogorov-Smirnov test was used to assess normal distribution of continuous variables. Independent t test was used to assess statistical significance between groups. The correlation of VAS and MIDAS values with RNFL and GCC thicknesses was assessed by Pearson's correlation coefficient. A p value <0.05 was considered as statistically significant.

RESULTS

Mean age was 36.05±8.84 years in migraine group and 32.89±10.89 years in control group. There was no significant difference in age and sex distributions between groups (p=0.117 and p=0.275, respectively). Mean time of follow-up was 5.50±3.42 years in patients with migraine. Table 1 presents demographic characteristics of all subjects.

No significant differences were detected in mean RFNL and GCC thicknesses from all quadrants between migraine and control groups (p>0.05 for all) (Table 2).

It was found that VAS scores were negatively correlated to mean RNFL thicknesses and those in temporal and inferior quadrants (p=0.036, p=0.010, p=0.021, respectively) (Table 3). Similarly, It was found that MIDAS scores were negatively correlated to mean RNFL thicknesses and those in temporal and inferior quadrants (p=0.045, p=0.026 and p=0.023, respectively) (Table 4).

Table 1. Characteristics of migraine and control groups

		Migraine (44)	Control (54)	p
Age (year)		36.05±8.84	32.89±10.89	0.117*
Sex	Male	6 (%14)	12 (%22)	
	Female	6 (%14)	12 (%22)	0.275**
Migraine duration (years)		5.50±3.42	-	
Number of migraine attacks/month		3.18 ± 0.94	-	
Duration of migraine attack (hours)		28.09±12.32	-	
VAS		8.18±0.78	-	
MIDAS		3.18±0.89	-	

*=Student's t-test **=Chi-square test, VAS: Visual Analogue Scale, MIDAS: Migraine Disability Assessment

Table 2. Median OCT analysis results of the groups

	Migraine	Control	p*
RNLF overall (µm)	98.31±21.80	95.59±9.96	0.426
RNLF superior (µm)	121.47±29.88	119.02±17.86	0.627
RNLF temporal (µm)	72.17±25.12	68.02±12.66	0.304
RNLF inferior (µm)	132.39±23.84	125.17±19.91	0.123
RNLF nasal (µm)	69.64±20.37	72.09±10.80	0.459
GCC superior (µm)	82.01±11.69	83.85±6.73	0.346
GCC inferior (µm)	81.44±11.27	84.16±6.78	0.157

*=Student's t-test, RNFL: Retinal nerve fiber layer. GCL: Ganglion cell complex

Table 3. Correlation between VAS score and OCT analysis results among migraine patients

	VAS	
	r	p*
RNLF overall (µm)	-0.350	**0.036**
RNLF superior (µm)	-0.129	0.452
RNLF temporal (µm)	-0.426	**0.010**
RNLF inferior (µm)	-0.383	**0.021**
RNLF nasal (µm)	-0.181	0.292
GCC superior (µm)	0.052	0.761
GCC inferior (µm)	0.125	0.466

*=Pearson correlation, VAS: Visual Analogue Scale, RNFL: Retinal nerve fiber layer. GCL: Ganglion cell complex

Table 4. Correlation between degree of disability and OCT analysis results among migraine patients

	MIDAS	
	r	p*
RNLF overall(µm)	-0.336	**0.045**
RNLF superior (µm)	-0.283	0.095
RNLF temporal (µm)	-0.371	**0.026**
RNLF inferior (µm)	-0.379	**0.023**
RNLF nasal (µm)	-0.175	0.306
GCC superior (µm)	-0.092	0.595
GCC inferior (µm)	0.114	0.509

*=Pearson correlation, MİDAS: Migraine Disability Assessment RNFL: Retinal nerve fiber layer. GCL: Ganglion cell complex

DISCUSSION

Many anatomists consider retina with its receptors, ganglion cells, glial support cells and axons as an extension of brain. The RNFL have similar features with gray matter in brain and changes in its thickness are solely related to axonal injury. In this perspective, it is thought that retina is a readily observable part of brain.

It is known that vasospasm occurring before or during headache also present in extra-cerebral tissues and causes histopathological and functional changes at tissue level (12,13). Papillary blood supply is provided by choroidal arteries, posterior ciliary artery and pial vessels innervated by trigeminal nerve. Thus, migraine attack can also cause damage in RNFL and GCC layer by alterations in papillary and retinal vascularization.

In their study, Martinez et al. found that temporal quadrant RNFL thickness was lower in patients with migraine when compared to healthy controls and that there was further thinning in RNFL in cases with higher MIDAS scores in migraine group. In that study, MIDAS score was used to assess pain severity in patients with migraine and it was found that there was a negative correlation between RNFL thickness and MIDAS scores (4). In a study by Gipponi et al., it was found that RNFL thicknesses at superior quadrants were significantly lower in patients with migraine than controls. When compared according to disease duration (disease duration >15 years or <15 years) and attack frequency (>4 attacks per month or <4 attack per month), no significant difference was detected in RNFL thickness between groups (13). In a study on 39 patients with migraine (15 patients with MwA and 24 patients with MwoA), Tan et al. found that there was no significant difference in RNFL thickness in patients with migraine when compared to healthy individuals (14). In our study, peripapillary RNFL thickness was similar between the migraine group and the control group. The short duration of migraine disease may explain the ineffectiveness of ocular structures. The short duration of migraine disease may explain the lack of thinning in ocular structures. It was found that MIDAS and VAS scores were negatively correlated to mean peri-papillary RNFL thickness and RNFL thicknesses at temporal and inferior quadrants. The correlation analysis indicated that migraine severity might have significant effect on changes in ocular structures.

It is thought that there may be retrograde trans-synaptic degeneration that may have influence on retinal GCC layer (15). In their study, Ekinci et al. investigated the relationship between RNFL and GCC layer and migraine subtypes and they found that there were significant thinning in RNFL and GCC layer in all quadrants other than nasal quadrant in patients with MwA when compared to controls. No such relationship was shown between patients with MwoA and controls (15). Reggio et al. found that GCC layer was thinner in chronic migraine when compared to healthy individuals (16). In a study by Çolak et al., GCC layer was compared between patients with MwA and healthy individuals. Authors found that superior and inferior GCC layer thicknesses were comparable among groups (17). Similarly, no significant difference was found in peri-foveal GCC layer thickness between migraine and control groups in our study. No correlation was found between GCC thickness measured on OCT and MIDAS or VAS scores.

CONCLUSION

No significant difference was detected in peri-papillary RNFL and GCC thickness in migraine patients when compared to healthy individuals. No significant correlation was detected between GCC layer thickness and MIDAS or VAS score while mean, temporal and inferior RNFL thicknesses were found to be negatively correlated to MIDAS and VAS scores. In the literature, there are contradictory results in this issue. Further studies are warranted. We believe that future studies using OCT angiography will be helpful to reveal effects of migraine on retina and choroid vascular system.

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