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Peripapillary Retinal Nerve Fiber Layer Thickness in Patients with Chronic Migraine

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Abstract
Purpose: *To evaluate thickness of the peripapillary retinal nerve fiber layer (RNFL) by optical coherence tomography (OCT) among subjects with migraine headache and to compare it with healthy subjects.*
Materials and Methods: *This is a prospective cross-sectional study of 65 subjects with chronic migraine headache, aged between 18 and 40 years and 65 healthy subjects of same age group without headache as control group., Intraocular pressure (IOP) and axial length (AL) were measured in each case of both the study groups. Peripapillary RNFL was measured using OCT in all participants and then it was compared between migraine and control group.*
Results: *In this study, mean age of the participants was 31.84±6.03 years in migraine headache group and 31.69±5.94 years in control group. The mean duration of migraine in patients after diagnosis was 7.84±6.03 years. The average peripapillary RNFL thickness was 95.84±6.03 µm in migraine headache group and 97.32±7.08 µm in control group. The mean superior quadrant RNFL thickness was 115.84±13.03 µm in migraine headache group, 121.85±14.72 µm in control group. The average peripapillary RNFL thickness and the superior quadrant thickness was statistically significant different between migraine and control groups (p =0.0031, p =0.0150 respectively).The measurements of the RNFL thickness in inferior, temporal and nasal quadrant were not statistically significant between migraine and control groups.*
Conclusion: *The average and superior quadrant peripapillary RNFL were thinner in patients with chronic migraine than the healthy participants.*
Keywords: *Migraine, Optical Coherence Tomography, Peripapillary RNFL.*

Introduction

The pain located above orbitomeatal line is termed as headache.[1] Headache is a universal experience and lifetime prevalence has been suggested as 99% in the literature.[2] Headaches are more prevalent in India as elsewhere in the world. Most of the patients of headache are underdiagnosed and undertreated. Headaches are often associated

with significant drop in quality of life.[3] Considering the high prevalence and negative impact on life, headaches are currently considered as a public health problem.[4] Headache can be divided into primary and secondary headaches. Primary headaches are divided into migraine and tension–type headache. Secondary headaches include conditions of other etiologies. Kulkarni et al had estimated the prevalence of migraine to be 25.2% in Karnataka state of India.[5] The prevalence of primary headache varies 9-11% in India.[3,6,7]

Primary headaches don't have any structural, metabolic or other lesion of the body whereas secondary headaches have some exogenous disorders. The migraine headache has been ranked as third most prevalent disorder and placed seventh among the top ten causes of disability worldwide in the Global Burden of Disease Survey 2010 (GBD2010). According to Headache Classification Committee of the International Headache Society[1] the migraine headaches are of two subtypes–

A. Migraine without aura, a clinical syndrome characterized by headache with specific features and associated symptoms

B. Migraine with aura characterized by transient focal neurological symptoms which precede or sometimes accompany the headache.

Episodic migraine is defined as 0-14 attacks of headache days per month and chronic migraine is defined as 15 or more attack of headache days per month.[1] Although the etiology of migraine is unknown, several studies have shown diminished cerebral blood flow during migraine attacks in the occipital hemisphere and also hypoperfusion of retina and optic nerve resulting in ganglion cell loss.[8.9] The retinal nerve fiber layer (RNFL) contains the axon of the retinal ganglion cells.

The chronic attacks of migraine which is characterized by recurrent vasospasms and focal ischemia could explain structural optic nerve and retina damage with subsequent reduction in peripapillary RNFL.[10,11]

OCT is a reliable reproducible noninvasive transpupillary diagnostic imaging that utilizes infrared wavelengths and enables quantitative in vivo high resolution measurement of peripapillary RNFL. Decreased thickness of RNFL has been reported in the literature for various neurological disorders.[12-14] Therefore, considering migraine headache, a serious burden to a clinician, this study was aimed to measure and compare the thickness of peripapillary RNFL by OCT in patients with migraine and in healthy individuals, that will improve our understanding of pathophysiology of migraine and follow up of effective migraine therapy.

Materials and Methods

This is a cross-sectional study of 65 patients diagnosed to have diagnosis of migraine according to 2010 criteria of the International Headache Society between 18 and 40 years in the medicine department and age-matched 65 healthy subjects from ophthalmology department without headache as control group. The study was conducted over a period of one year from January 2018 to December 2018 in the ophthalmology outpatient department (OPD). A detailed history of headache was obtained from each patient. Physical and neurological examinations were done. We included consecutive patients who were referred from the medical OPD with diagnosis of chronic migraine headache aged between 18 and 40 years. This research protocol was approved by the Institutional ethics committee. All the investigations were done according to Helsinki declaration. The full informed consent was taken from all participants.

The study group and control group were interviewed with structured questionnaires about demographic data. Those having other types of headache were excluded from the study. The participants in the study group were then asked about frequency, duration, severity and intensity of headache. It also included presence of any aggravating factors, family history and history of trauma, medical history, dental caries, features of

raised intracranial pressure, menstrual disturbances, previous ocular surgeries and use of medicines. The cases with systemic diseases, sinusitis, and intake of medicines, dental caries that cause headache or ocular conditions like refractive error, optic neuritis, normal tension glaucoma and maculopathies were excluded from the study. We also excluded patients of multiple sclerosis, Alzheimer disease, Parkinson disease,

Complete ophthalmological examination, slit lamp biomicroscopy and fundus examination were done to rule out any anterior or posterior segment ocular pathology. Ocular motor functions were evaluated in six cardinal gazes. Intraocular pressure was measured with Goldman tonometer.

The thickness of peripapillary RNFL was measured by 360º circular scanning around the optic nerve with 3D OCT after dilatation of the pupils with 0.5% tropicamide solution in patients with chronic migraine and in healthy individuals to compare between the two groups. The RNFL thickness parameters calculated by the OCT software (version 8.42.003.01) were averaged for thickness in the superior, inferior, temporal and nasal quadrants. Statistical analysis was done with software SPSS version 20.0 to analyze the data of the study. P-value less than 0.05 were considered statistically significant level.

Results

A total of 65 subjects with diagnosis of migraine headache and 65 without headache as control normal group participated in the study. It included 9 (13.8 %) females and 56(86.2 %) males in migraine headache group and 10(15.4 %) females and 55(84.6%) males in control group. Mean age of the participants was 31.84±6.03 years in migraine headache group and 31.69±5.94 years in control group. The mean duration of migraine in patients after diagnosis was 7.84±6.03 years. The mean intra ocular pressure (IOP) in the patient with migraine was 14.84±4.03 mm of Hg and 14.13±3.9 mm of Hg in the control group. The IOP in subjects with migraine headache group and in controls was statistically insignificant (p =0.3093). The mean axial length (AL) was 23.3±0.8 mm in migraine and 23.4±0.6 mm in control group. The difference of axial length was not statistically significant between two groups (p=0.4216) (Table-1).

On optic nerve head (ONH) evaluation the mean cup to disc ratio (CDR) in migraine group was 0.56±0.09 and in control group 0.57±0.11. The difference was not statistically significant between two groups (p=0.5715).

The average RNFL thickness was 95.84±6.03 µm in migraine headache group and 97.32±7.08 µm in control group. The average RNFL thickness was statistically significantly different between migraine and control groups (p =0.0031).The mean superior quadrant RNFL thickness was 115.84±13.03 µm in migraine headache group and 121.85±14.72 µm in control group. The measurements of the RNFL thickness in superior quadrant was statistically significantly different between migraine and control groups (p =0.0150).

The measurements of the RNFL thickness in temporal quadrant was 70.37±9.5 and 70.56±10.16 between migraine and control groups respectively were not statistically significant different. (p =0.6411). The mean RNFL thickness in inferior quadrant was 125.33±11.33 in migraine and 128.24±14.27 in control group. The mean RNFL thickness in nasal quadrant was 69.11±11.0 in migraine and 70.56±10.16 in control group. The measurements of the RNFL thickness in inferior and nasal quadrant were not statistically significant between migraine and control groups. (p =0.2002, p=0.4364 respectively) (Table- 2).

Table-1: Baseline demographic characteristic with intraocular pressure and axial length

Variables		Migraine patients	Controls	P value
Age in years, mean (SD)		31.84(6.03)	31.69(5.94)	0.8866
Sex	Male	9(13.8%)	10(15.4%)	
	Female	56(86.2%)	55(84.6%)	
IOP mm of Hg, mean (SD)		14.84(4.03)	14.13(3.9)	0.3093
Axial length in mm(SD)		23.3(0.8)	23(0.6)	0.4216

Table-2: Comparison of optic nerve head (ONH) and retinal nerve fiber layer (RNFL) thickness in migraine patients and control group

	Variable	Migraine group Mean (SD)	Control group Mean (SD)	P value
Optic nerve head(ONH)	Average cup to disc ratio(CDR)	0.56(0.09)	0.57(0.11)	0.5715
Retinal Nerve Fiber Layer (RNFL)	Average	93.84(6.03)	97.32(7.08)	0.0031
	Superior	115.84(13.03)	121.85(14.72)	0.015
	Inferior	125.33(11.33)	128.24(14.27)	0.2002
	Nasal	70.37(9.5)	70.56(10.16)	0.4364
	Temporal	69.11(11.0)	71.13(9.04)	0.6411

Discussion

One of the theories of mechanism of migraine is focal brain hypoperfusion in posterior circulation that involves other parts of the brain and retina. RNFL thickness measurements can be used as an index to assess ganglion cells and retinal nerve fiber damages. RNFL thickness measurement by OCT is a reliable and reproducible technique for evaluation of retina.

In our study, the average RNFL thickness of 95.84(6.03) µm in patients with migraine was found to be statistically significantly thinner compared to 97.32(7.08) µm of the control group (p=0.0031). In the superior quadrant RNFL thickness was 115.84 (13.03) µm in migraine headache group and 121.85(14.72) µm in control group. The measurements of the RNFL thickness in superior quadrant was statistically significantly different between migraine and control groups (p =0.0150). Kirbas et al[15] and Gipponi et al[10] also reported significantly thinner RNFL thickness in superior quadrant in migraine patients compared to the controls. Colak HN et al[16] reported thinner RNFL thickness in superior and inferior quadrant in migraine patients compared to the controls.

In this study, there was no statistically significant difference in the RNFL thickness measurement of inferior, temporal and nasal quadrant RNFL between two groups, but in the study of Martinez et al[5] in Spain out of 70 migraine patients and 53 healthy controls, the temporal quadrant RNFL thickness was significantly reduced in migraine patients than to the normal controls. In the study of Sorkhabi R et al[17] in Iran of 60 migraine patients and 30 controls significant difference in nasal quadrant RNFL thickness was reported, though in our study we didn't find any statistical difference between the two groups.

Conclusion

We found that the average thickness of RNFL and superior quadrant RNFL thickness was reduced in migraine patients compared with those of age and sex matched control group. In the review of literature, we found, authors have reported discrepant results of RNFL thinning in different quadrant of migraine patients. Therefore further investigations are needed to establish a definite correlation of RNFL thinning and migraine headache. The measurement of RNFL by OCT in migraine patients could be a useful technique for the better understanding of migraine pathogenesis.

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Conflict of Interest: None

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