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RETINAL BIOMARKERS IN MIGRAINE USING OPTICAL COHERENCE TOMOGRAPHY –A STUDY FROM TERTIARY CENTER IN SOUTH INDIA

Neurology

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ABSTRACT

Migraine is one of the most prevalent primary headache disorder. In this study we used Optical Coherence Tomography (OCT) to measure the retinal thickness .We noticed significant thinning in thickness of retinal nerve fiber layer , ganglion cell layer and macula in patients with migraine with correlation to the duration and severity of migraine. This study shows that OCT can be used as biomarker in migraine to assess adequacy of existing treatment and to develop targeted newer therapies in migraine.

KEYWORDS

Migraine, Optical Coherence Tomography (OCT), Ganglion cell layer, Retinal nerve fiber layer

INTRODUCTION

Migraine is episodicpulsatile unilateral headache associated with nausea or vomiting and sensitivity to light and sound. Migraine is the most common neurological disorder with a high prevalence and morbidity especially among young adults and females(1). In India, more than 10 million cases are reported every year. It has great psychological and socio-economic burden on patients. The trigeminovascular system (TGVS) plays an important role in pathogenesis of migraine (2).TGVS regulates vascular tone and is responsible for transmission of pain signals. Optical Coherence Tomography (OCT) is a non-invasive imaging technique based on the principle of low-coherence light interferometry (3, 4). OCT images are two dimensional which represent optical back scattering in cross sectional plane through the tissues .OCT helps in measuring the total retinal thickness and retinal nerve fiber layer thickness. Our study aims to correlate the changes in retinal nerve fiber layer (RNFL) (peripapillary and macular), ganglion cell layer (GCL) with the severity and duration of migraine and to evaluate role of OCT as biomarker in migraine.

AIMS AND OBJECTIVES

1. To evaluate the role of OCT as biomarker in assessment of migraine.
2. Compare the thickness of the retinal nerve fiber layer (RNFL), macula, and ganglion cell layer (GCL) in the eyes of migraine patients with healthy subjects using optical coherence tomography (OCT).
3. Correlate the severity and duration of migraine (in years) with RNFL, GCL and macula thickness

METHODOLOGY: MATERIALS AND METHODS

This is an observational case -control study with a sample size of 100 conducted at Dr PSIMS & RF Neurology OP department for 2 months 100 cases (200 eyes) of migraine selected according to ICHD3 (beta) criteria with inclusion and exclusion criteria as below

Inclusion criteria

Patients with migraine >18 years of age - < 60 years of age.

Exclusion criteria

Previous ocular trauma, intraocular surgery, cataract, glaucoma, strabismus, eccentric fixation, laser treatment , organic eye diseases, neurological disorders, retinal or optic nerve disorders, and diabetic or hypertensive retinopathy.

The control group consisted of 50 age and sex matched healthy controls (100 eyes).

All the patients are evaluated with spectral domain optical coherence tomography. Average macular thickness, optic disc parameters such as retinal nerve fiber layer thickness, ganglion cell layer thickness is analyzed. Scans for all participants were performed with pupillary dilatation under the same intensity of dim room lighting by the experienced professional.

MIDAS Questionnaire is used to assess the severity of migraine (grade 1 to grade 4). Written informed consent for participation in the study was obtained from each patient.

RESULTS

This study included both eyes of 100 patients (200eyes) and 50 healthy controls (100 eyes).

The mean ages were 33.03±11.12 and 34.48±10.86 for migraine patients and healthy controls respectively. The mean attack frequency was 16.04 ±6.96 days per month in migraine patients. (Table 1)

Table – 1:

Variable	Control (n = 50)	Migraine patients (n = 100)
Age (years)	34.48±10.86	33.03±11.12
Gender (male/female)	13(26%)/37(74%)	32(32%)/68(68%)
Involved side (right/left)	—	43/57
Number of migraine attacks/month	—	16.04±6.96

Values are expressed as mean ± SD

We compared the average Retinal nerve fiber layer thickness (RNFL) and ganglion cell layer thickness (GCL) and macular thickness in migraine patients with healthy controls. There was significant difference in the average thickness of Retinal nerve fiber layer of both eyes (right eye p=<0.001; left eye p=0.002) (Table – 2) and in the thickness of ganglion cell layer (right eye p<0.001, left eye p=0.002) (Table – 3) in migraine patients to that of controls. Similarly the average macular thickness was significantly less in migraine patients compared to the healthy controls (p<0.001 in both eyes).(Table – 4)

Table-2 : Comparison Of The Average Retinal Nerve Fiber Layer (RNFL) Thickness (µm) Of The Migraine Patients And Control Groups.

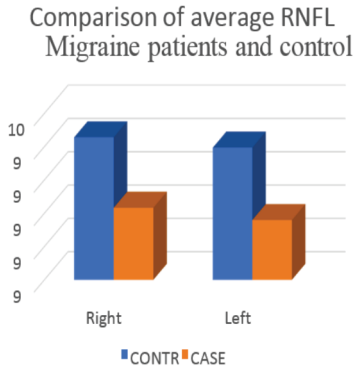
Variable	Control (n=50)	Migraine patients (n=100)	T value	P value
RNFL-Right eye	98.56 ±6.41	94.33±7.21	-3.66	<0.001*
RNFL-Left eye	97.94 ±6.76	93.59±7.12	-3.65	<0.001*

T value is calculated using independent t test Values are expressed as mean ± SD

Table – 3: Comparison Of Ganglion Cell Layer Thickness (GCL) (µm) Of The Migraine Types And Control Groups.

Variable	Control (n=50)	Migraine patients (n=100)	T value	P value
CL -Right eye	83.7 ±3.87	80.17 ±5.49	-4.55	<0.001*

GCL- left eye	83.4 ±3.57	81.06 ±5.52	-3.13	0.002*



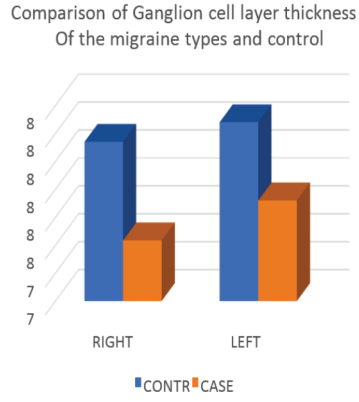
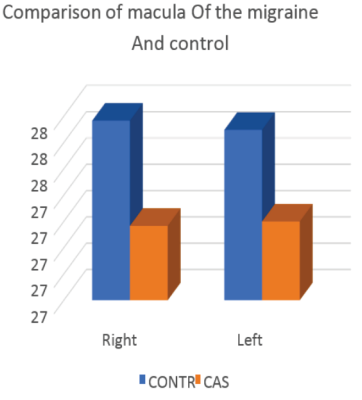


Table – 4: Comparison Of Macular Thickness (µm) Of The Migraine Types And Control Groups.

Variable	Control (n=50)	Migraine patients (n=100)	T value	P value
Macula- right eye	283.66 ±7.1	275.66 ±9.87	-5.7	<0.001*
Macula-left eye	282.96 ±6.31	275.99 ±9.82	-5.25	<0.001*

T value is calculated using independent t test Values are expressed as mean ± SD



We compared the duration of migraine (in years) with RNFL, GCL, and Macula thickness. There was significant thinning of RNFL, GCL, and Macula with increase in duration of migraine, increase in thinning was noticed in patients with > 1year of migraine with average RNFL thickness of 93.3±7.91 and 93.13±8.02 in right and left eye respectively (Table – 5). Thinning of macula was predominant in left eye in group with duration of migraine >1year (p=0.02) which correlated with the laterality of headache (Table – 6).

Table – 5 : Comparison Of Duration Of Migraine And Retinal Nerve Fibre Layer Thickness

Variable	Duration of migraine (in years)		T value	P value
	<=1	>1		
RNFL-Right eye	96.75±6.94	91.82±6.65	3.63	<0.001*
RNFL-Left eye	96.39±6.04	90.67±7.03	4.35	<0.001*

F value is calculated using ANOVA test Values are expressed as mean ± SD

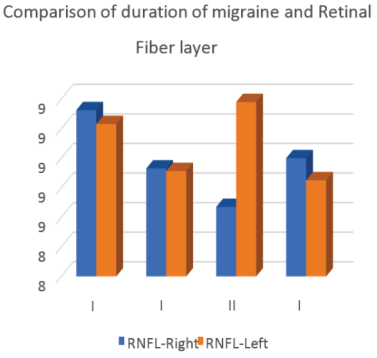


Table – 6: Comparison Of Duration Of Migraine And Macular Thickness

Variable	Duration of Migraine (in years)		T value	P value
	<=1	>1		
Macula-Right eye	277.45±9.69	273.8±9.81	1.87	0.06
Macula-Left eye	278.98±9.2	272.88±9.55	3.25	0.002*

T value is calculated using independent t test Values are expressed as mean ± SD

Similarly there was a gradual decrease in the average thickness of macula with increase in severity of migraine (right eye p 0.001, left eye p 0.002)

Comparison of severity of migraine and macula showed least thinning in migraine patients with grade I severity with and severe thinning in grade IV patients with right eye(p-0.001),left eye (p-0.002) (Table – 7).

Table – 7: Comparison Of Severity Of Migraine And Macula Thickness

Variable	SEVERITY OF MIGRAINE				F value	P value
	I	II	III	IV		
Macula-Right eye	281.2± 9.9	284.71± 5.37	276.35 ±10.01	271.31± 8.23	6.19	0.001*
Macula-Left eye	284.2± 9.15	283.29± 7.04	275.35± 9.33	273.06± 9.44	5.35	0.002*

F value is calculated using ANOVA test Values are expressed as mean ± SD

However the RNFL thickness did not show any correlation with the severity of migraine (right eye p=0.06,left eye=0.09)

DISCUSSION

Migraine can be episodic or chronic based on the frequency of attacks. Various vascular, cellular, hormonal theories have been proposed of which trigeminovascular system activation plays a major role in the pathophysiology of migraine(5,6,7,8) Atypical pain processing ,cortical hyper excitability ,neurogenic inflammation and central sensitization are involved in migraine pathophysiology . Alternating episodes of change in vascular caliber lead to hypo perfusion and hyper perfusion both in cerebral and extra cerebral sites like retina .Recurrent episodes of transient vasoconstriction can lead to permanent cerebral and retinal damage (9, 10, 11) Several functional and structural changes in brain have been noticed which correlate with the duration and frequency of disease.There are various studies on the effects of vasospasm and ischemia on the retina and optic nerve head. Kara et al(12) used colored Doppler ultrasonography and found a reduction in blood flow at the level of the central retinal artery and posterior ciliary artery in migraine patients, compared to healthy individuals.OCT is simple noninvasive means to evaluate the retina and optic nerve (13,14). Our study showed significant difference in the thickness of RNFL(macular and peripapillary),ganglion cell layer in patients with migraine compared to controls which is similar to other studies(15,16) We noticed decrease in thickness of RNFL,GCL of both eyes in multiple quadrants .Abdellatif et al documented a decrease in all quadrants of retinal nerve fiber layer of the eye of migrainous patients(17,18). In our study we also noticed a significant thinning in unilateral macula (left side) correlating with the side of migraine headache Gunes et al (19) also noticed significant thinning which

correlated with laterality of migraine which he explained as the greater loss of thickness in the same eye could be due to the decrease in blood flow from the retina in the homolateral eye as a result of the migraine.

Our study showed that the patients with less than 1 year of migraine had significantly lesser thinning of the RNFL compared to those with more than one year of duration. The chronicity of migraine with recurrent episodes of vasospasm leading to focal ischemia may explain the decrease in RNFL thickness (20).Feng et al described marked decrease in the mean value of RNFL thickness in patients with longer duration of migraine (21). Few studies showed no correlation between the duration and RNFL,GCL thickness (22).Our study showed significant thinning in macular RNFL compared to peripapillary RNFL layer with the increase in severity of migraine .We noticed no significant correlation between peripapillary RNFL thickness to the severity of migraine with p values (right eye0.06,left eye=0.09). GCL also showed siginificant decrease in thickness with increasing severity which also correlated with the side of headache .Many studies have reported significant correlation between the severity and RNFL thickness while some have shown no relation which may be likely due to the different scoring systems used and differences in the study groups.

CONCLUSION

This study shows that thinning of the retinal layers correlate with the duration and severity of migraine which may be attributed to neurovascular pathogenesis of migraine. Early treatment within one year of diagnosis of migraine may prevent further retinal thinning.Targeting specific aspects of the vascular system may help in developing new therapies in migraine .OCT can be used as biomarker in migraine by monitoring the retinal changes which may help in assessing the adequacy of existing treatments and development of newer therapies in migraine .

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