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Assessment of optic disc and macula in fasting period during Ramadan by optical coherence tomography angiography

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Abstract

Aim: The aim of this study is to assess the effect of fasting on the ultrastructure and vascular density of the optic disc and macula by optical coherence tomography angiography (OCT-A).

Materials and Methods: 38 eyes of 19 healthy subjects were enrolled in this study. AngioVue OCT-A images of optic disc and macula were taken during fasting and non-fasting periods. Retinal nerve fiber layer (RNFL) thickness, radial peripapillary capillary vessel density (VD), central macular thickness (CMT), macular superficial, deep and choroid capillary plexus VD, foveal avascular zone (FAZ), acircularity index of foveal avascular (AI), foveal density (FD) zone were compared.

Results: No statistically significant difference was found between the two periods in terms of RNFL thickness, radial peripapillary capillary VD. Parafoveal superficial macular VD was significantly reduced in fasting period than non-fasting period (46.21% ± 5.71% & 48.15% ± 4.45% p= 0.039). Whole image, parafoveal and perifoveal total retinal VD was significantly decreased in fasting period than non-fasting period (49.46% ± 4.28% & 50.88% ± 3.43% p=0.029; 52.38% ± 5.85% &54.60% ± 3.74% p= 0.012; 49.99% ± 4.58% & 51.35% ± 3.40% p= 0.030). CMT, deep retinal VD, choriocapillary VD, FAZ area, FAZ perimetry, AI, FD and nonflow area were not statistically different in fasting and non-fasting periods ($p > 0.05$).

Conclusion: Fasting during Ramadan causes alterations in retinal microcirculation.

Introduction

Fasting is one of the five pillars of Islam, Muslims fast in the month of Ramadan. Islamic fasting means not to eat and drink anything from predawn to sunset. Ramadan is the 9th month in the lunar calendar. Since the lunar calendar consists of 354 days, the next Ramadan comes 11 days before the previous one and the season of fasting changes every 9 years. The fasting period may vary between 12-18 hours [1].

Especially in summer Ramadan, with the prolonged fasting period, some physiological changes occur in the body in the following hours. Hypoglycemia, dehydration, decrease in insulin secretion, increase in glucagon secretion and sympathetic system activation occurs. Increase of norepinephrine and cortisol levels, changes in lipid profile and electrolytes may affect choroidal, retinal and optic nerve blood flow and vessel density [2-4].

Optical coherence tomography angiography (OCT-A) is a new imaging modality that rapidly and noninvasively displays retinal and choroidal vascular structures without dye injection. Changes in erythrocyte movements are displayed with multiple B-scan images taken with OCT-A. It quantitates the measurements by segmentation of the retina and enables the visualization of the radial peripapillary capillary layer, superficial and deep retinal vascular plexus, choriocapillaris [5].

The aim of this study is to evaluate the changes in the microcirculation of the optic disc and retina, caused by fasting in the month of Ramadan with OCT-A. Although there are studies evaluating the retinal and peripapiller microcirculation in Ramadan [6-9], the results are contradicting.

Materials and Methods

This prospective study was conducted in a tertiary level hospital in Ankara. The study was approved by the local ethical committee of the Ankara City Hospital (E1-20-924) and the study protocol adhered to the Declaration of Helsinki. Written informed consent was obtained from all

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participants. Sample size was determined by using Power analyses. At the 0.5 effect size, 5% error level; at least 36 observation units were needed to reach the 0.90 power level. Healthy volunteers, aged between 18-65 years with no known systemic disease, and who fasted in Ramadan were included in the study. Exclusion criteria were any systemic and ocular disorders including diabetes, hypertension, age related macular degeneration, glaucoma; history of ocular surgery and a refractive error of $> \pm 3$ spherical equivalent, using a drug that can change the vessel diameter before the examination day. Detailed ophthalmological examinations including assessment of refraction and visual acuity, slit lamp biomicroscopy, air puff tonometry and fundus imaging were performed to all participants. Volunteers with 20/20 visual acuity, normal anterior and posterior segment examination, and intraocular pressure $<$21 mm Hg were included in the study.

OCT-A imaging of optic disc and macula was performed by the same technician, between 2.00 pm and 4.00 pm, after at least 10 hours of fasting. An internal fixation target was used to focus the eye. Images with appropriate quality were included in the study. The participants were evaluated again with OCT-A one month after the end of Ramadan in non fasting condition between 2.00 pm and 4.00 pm.

OCT-A images were taken with RTVue-XR Avanti (Optovue, Inc., Fremont, CA, USA) which is a spectral-domain optical coherence tomography (SD-OCT) system. The instrument performs quantitative analysis with the Split Spectrum Amplitude-Decorrelation Angiography (SSADA) algorithm. Vessel density (VD) is a quantitative indicator of the percentage of vessels with flow in a certain area over the whole area. VD was given automatically by the instrument. Three-dimensional (3D) OCT angiography of the optic disc were acquired using a 3 $\times$ 3-mm scanning area. Retinal nerve fiber layer (RNFL) thickness and radial peripapillar capillary (RPC) VD in the whole image, inside disc, peripapillary (superior and inferior) areas were obtained automatically.

A scanning area of 6 mm $\times$ 6 mm centered on the fovea was used for macular analysis. Central macular thickness (CMT); whole, foveal, parafoveal and perifoveal VDs in the superficial capillary plexus (SCP), deep capillary plexus (DCP) and choriocapillary area; nonflow area in SCP, free avascular zone (FAZ) area, FAZ perimetry, acircularity index (AI), foveal density (FD 300) and nonflow area values were recorded.

The primary endpoint measurements of this study were the difference of macular and optic disc vascularity via OCTA, between fasting and non-fasting state.

Statistical analysis

The statistical software package SPSS 18.0 (SPSS Inc., Chicago, Illinois, USA) for windows was used for data analysis. Data distribution for normality was assessed using Kolmogrow Smirnov test. Paired t-test or Wilcoxon test was used to determine the differences between the measurements. Data were presented as mean $\pm$ standard deviations. A p value of $<$0.05 was considered statistically significant.

Results

Thirty-eight eyes of 19 patients (8 male, 11 female) were included in the study. The mean age was 43.58±10.04 years (25-56).No statistically significant difference was found between the two periods in terms of RNFL thickness and RPC VD (Table 1). Parafoveal SCP VD was significantly reduced in fasting period than non-fasting period (46.21 ± 5.71&48.15 ± 4.45 p=0.039). Whole image, parafoveal and perifoveal total retinal VD was significantly decreased in fasting period than non-fasting period (49.46% ± 4.28% & 50.88% ± 3.43% p= 0.029; 52.38% ± 5.85%&54.60% ± 3.74% p= 0.012; 49.99% ± 4.58% & 51.35% ± 3.40% p= 0.030). Central macular thickness, deep retinal VD, choriocapillary VD, FAZ area, FAZ perimetry, AI, FD and non-flow area were not statistically different between fasting and non-fasting periods ($p > 0.05$) (Table 2 and Table 3).

Discussion

Ramadan is a holy month when Muslims fast. Eating and drinking are prohibited from the time of predawn until the sunset in Ramadan. Changes in eating, drinking and sleeping habits lead to improvements in systemic blood pressure, lipid profile and insulin resistance, and increase in glucagon, norepinephrine and cortisol levels. Fasting causes changes in blood osmolarity and serum electrolyte levels [10, 11]. Physiological changes caused by fasting lead changes in anterior and posterior segment of the eye. Tear and intraocular pressure, refractive and topographic changes, retinal and choroidal thickness changes have been reported due to fasting [12-14]. Ocular blood flow is also affected by systemic parameters and electrolyte levels, so fasting affects blood flow and vascular density of the retina, choroid and optic disc [2-4]. Blood supply to the retina is provided by central retinal artery (CRA) and choroid blood vessels. While the choroid vessels supply especially to the outer retina (photoreceptor layer), branches emerging from the CRA supply blood to inner retinal layers as 3 capillary networks: 1.RPC, 2.Inner capillaries 3. Outer capillaries. RPCs are the most superficial capillaries, lie within the nerve fiber layer. Inner capillaries are located in the ganglion cell layer and the deeper capillary plexus is located in the inner nuclear layer. From the optic nerve head, retinal vessels lack autonomic innervations; local (metabolic, myogenic, etc.) control mechanisms are responsible in the blood flow of the retina. Autonomic (neural) and local mechanisms are responsible in the blood flow of the choroid [15, 16]. Blood supply to the optic nerve head is provided by the posterior ciliary and central retinal artery, while blood flow to the RNFL is provided by microcirculations from these two vessels and retinal RPCs [17]. There are studies evaluating the blood flow changes of the optic disc in the fasting conditions. In the study evaluating the retrobulber vessel blood velocity with color Doppler ultrasound, a statistically significant decrease in the blood flow in the ophthalmic artery, CRA, and temporal short posterior ciliary artery was noted in the fasting condition [18]. Alghadyan et al. showed that central retinal vein occlusions (RVO) increase during Ramadan. They suggested that dehydration may play a role in the pathogenesis of RVO (19). OCT-A provides high resolution images of the optic nerve head and macula, is similar

Table 1. Retinal nerve fiber layer thickness and peripapiller data in fasting and non-fasting state using optical coherence tomography angiography.

		Fasting period (n:38)	Nonfasting period (n:38)	p
Angiodisc RPC density (capillary) (%)	Whole image	50.40 ± 2.14	50.27 ± 1.92	0.692
	Inside disc	48.19 ± 6.00	49.56 ± 5.00	0.122
	Peripapillary	53.81 ± 2.90	53.73 ± 2.17	0.839
	Peripapillary sup	54.33 ± 2.29	54.09 ± 2.30 1	0.565
	Peripapillary inf	53.53 ± 2.76	53.34 ± 2.4	0.679
Angiodisc RPC density (all) (%)	Whole image	56.27 ± 2.44	56.37 ± 2.07	0.776
	Inside disc	57.43 ± 4.85	58.52 ± 4.20	0.140
	Peripapillary	59.58 ± 2.50	59.57 ± 2.05	0.982
	Peripapillary sup	59.96 ± 2.46	59.99 ± 2.22	0.938
	Peripapillary inf	59.19 ± 2.70	59.14 ± 2.14	0.899
RNFL (µm)		113.95 ± 11.43	113.34 ± 10.54	0.246
RNFLS (µm)		134.18 ± 15.22	133.84 ± 14.79	0.591
RNFLT (µm)		73.95 ± 7.79	73.53 ± 7.02	0.183
RNFLI (µm)		141.89 ± 26.06	143.00 ± 23.93	0.791
RNFLN (µm)		105.42 ± 15.11	103.32 ± 12.71	0.299

Values are stated as mean±standard deviation.

RPC : Radial peripapillary capillary RNFL: Retinal nerve fiber layer; RNFLS: Retinal nerve fiber layer superior; RNFLT: Retinal nerve fiber layer temporal; RNFLI: Retinal nerve fiber layer inferior; RNFLN: Retinal nerve fiber layer nasal.

Table 2. Retinal and choroidal data in fasting and non-fasting state using optical coherence tomography angiography.

		Fasting period (n:38)	Nonfasting period (n:38)	p
Central macular thickness (µm)		255.92 ± 21.88	256.74 ± 22.40	0.057
Superficial retinal vessel density (%)	Whole image	46.04 ± 4.18	47.16±3.53	0.100
	Fovea	19.70 ± 7.26	20.55 ± 7.60	0.145
	Parafovea	46.21 ± 5.71	48.15 ± 4.45	0.039*
	Perifovea	46.91 ± 4.15	47.82 ± 3.47	0.149
Deep retinal vessel density (%)	Whole image	46.60 ± 4.79	45.79 ± 4.61	0.400
	Fovea	36.56 ± 8.82	36.63 ± 9.25	0.906
	Parafovea	52.79 ± 4.17	52.18 ± 4.09	0.500
	Perifovea	47.39 ± 5.00	46.72 ± 4.89	0.514
Total retinal vessel density (%)	Whole image	49.46 ± 4.28	50.88 ± 3.43	0.029*
	Fovea	33.22 ± 7.72	34.56 ± 8.24	0.059
	Parafovea	52.38 ± 5.85	54.60 ± 3.74	0.012*
	Perifovea	49.99 ± 4.58	51.35 ± 3.40	0.030*
Choriocapillary vessel density (%)	Whole image	69.09 ± 2.90	69.06 ± 2.38	0.912
	Fovea	63.32 ± 5.84	64.11 ± 4.93	0.303
	Parafovea	67.73 ± 3.35	67.20 ± 3.27	0.214
	Perifovea	69.65 ± 2.91	70.01 ± 3.08	0.387

Values are stated as mean±standard deviation.

*Statistically significant. FAZ, foveal avascular zone; SCP, superficial capillary plexus.

even better than conventional fluorescein angiography and laser Doppler flowmetry [20]. It permits non-invasive three dimensional evaluation of retinal and choroidal vessels and calculates VD of superficial and deep retinal vessels and choriocapillaries [21, 22]. A decrease in the peripapillary capillary network has been shown in glaucoma patients with OCT-A (20). Also retinal capillary vessel densities decrease in the systemic diseases like diabetes [23]. In the present study RPC VD were not different between fasting and non-fasting conditions. Shokoohi-Rad et al. showed that RPC VD decreased significantly after 15 hours of fasting [8]. Nilforushan et al. showed an increase in RPC VD and a decrease in IOP in the evening hours compared to morning hours in a fasting state. They also showed that RPC VD decreases in fasting conditions compared to non-fasting state [9]. Demirtaş et al. showed a decrease in parafoveal and peripapillary VD throughout the day in fasting and non-fasting conditions but they did not show a difference between fasting and non-fasting conditions [24]. In this study, superficial VD in the parafoveal region and

Table 3. Retinal data in fasting and non-fasting state using optical coherence tomography angiography.

	Fasting period (n:38)	Nonfasting period (n:38)	p
FAZ area(mm²)	0.249 ± 0.12	0.246 ± 0.13	0.588
FAZ perimetry	1.86 ± 0.53	1.88 ± 0.49	0.531
Acircularity index	1.105 ± 0.04	1.107 ± 0.05	0.976
Foveal density (%)	49.27 ± 4.80	50.52 ± 4.46	0.098
Nonflow area, SCP(mm²)	0.52 ± 0.17	0.50 ± 0.16	0.307

Values are stated as mean±standard deviation.
FAZ, foveal avascular zone; SCP, superficial capillary plexus.

total retinal VD in whole image, parafovea and perifovea was found to be reduced in the fasting period. Analysis of deep retinal VD revealed no statistically significant difference ($p > 0.05$). Karakucuk et al. noted a significant decrease in superficial VD while reported no change in deep retinal VD concurring with the present study [6]. On the other hand Gokmen et al. reported no significant difference in superficial and deep retinal VD between fasting and non-fasting states [7]. Decreased retinal VD may be explained by the effect of dehydration and local autoregulatory mechanisms. In the current study RNFL thickness did not change in fasting and non-fasting states similar to other studies [8, 25]. The absence of change in RNFL thickness with fasting can be explained by the absence of a major blood supply of the RNFL [25]. In contrast to our study, Nilforushan et al. reported a significant reduction in RNFL thickness in fasting state [9]. We showed that the CMT were not significantly different after Ramadan compared to fasting period. Also Karaküçük et al. and Shokoohi-Rad et al. did not show a change in the CMT in the fasting state [6, 8]. Balk et al. reported that acute oral hydration does not cause a significant change in the thickness of the retinal layers at any time-point [26]. In this study, we also evaluated the effect of fasting on choriocapillary VD. We did not record a significant difference between fasting and non-fasting conditions. Although the effects of fasting on choroid thickness have been well studied, the effect of fasting on choriocapillary VD has not been reported in literature. Fujiwara et al. reported a positive correlation between choriocapillary VD and choroid thickness [27]. In a study by Sarwar et al. choricapillary VD showed diurnal variation like choroid and showed a positive correlation with the choroidal thickness [28]. Choroid thickness can be measured by EDI-OCT, but EDI-OCT gives one cross sectional image of the choroid [29]. Choroidal VD can be measured in a coronal section with OCTA (30). The effect of fasting on choroid thickness is controversial. Duru and Uyar et al. showed that choroid thickness was thinner in subfoveal region at 16.00 pm in the Ramadan than non-fasting state [12, 25]. Ersan et al. showed a thicker subfoveal choroid thickness in Ramadan [14]. Blanco-Garavito et al. did not show a difference in the subfoveal choroid thickness following acute water ingestion after 12 hours of fasting [31]. They suggested that choroidal thickness could be independent of hydration status in healthy subjects. Autoregulation is the maintenance of blood flow in the vascular bed despite changes in perfusion pressure. Traditionally it is said that choroid does not have autoregulation [32, 33]. However, it is reported that choroid blood flow is regulated by the changes in the systemic blood pressure and intraocular pressure. Myogenic and neurogenic mechanisms are responsible in the regulation of the choroid blood flow [34]. The innervations of the choroid vessels are more than the retina vessels [35]. Sympathetic and parasympathetic nerves are found in the choroid [36, 37]. This may suggest that the blood flow of the choroid and deep retinal vessels are less affected by systemic changes and the blood flow in these areas are more tightly regulated. Its purpose may be to protect the photoreceptor layer. The limitations of the present study were the small sample size, absence of the recordings of systemic blood pressure and inability to assess the degree of hunger and thirst. This study was carried out in May, when the weather is hot and the days are long. This gives an idea about the hunger and thirst level of the participants. This study evaluated the effect of fasting in healthy subjects, so the results of this study could not be generalized to the patients with retinal disease and glaucoma.

Conclusion

In conclusion; in this study SVD and total retinal VD decreased in fasting state while RPC VD, RNFL, CMT, DVD, CVD, FAZ area, FAZ perimetry, AI, FD, nonflow area did not change. Further studies with more participants should be planned to investigate the effects of fasting in systemic and ocular disorders.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Ethics approval

The study was approved by the local ethical committee of the Ankara City Hospital (E1-20-924).

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