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Evaluation of choroidal thickness in rosacea disease

Armagan Ozgur[a], Isa An[b,*]

[a]Şanlıurfa Training and Research Hospital, Department of Ophthalmology, Şanlıurfa, Türkiye
[b]Şanlıurfa Training and Research Hospital, Department of Dermatology, Şanlıurfa, Türkiye

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Abstract

Aim: Rosacea is a chronic inflammatory dermatological disease characterized with erythema, telangiectasias, papules and pustules that is seen more frequently in individuals with fair skin. Our purpose in this study is to compare choroidal measurements of rosacea patients with healthy individuals.

Materials and Methods: Right eyes of 30 patients with ocular rosacea and right eyes of 30 healthy participants matched in terms of age and sex were included in the study. Choroid thicknesses were measured manually using optical coherent tomography device from the central subfovea; from the temporal as 1000 µm horizontally from the fovea and from the nasal.

Results: Subfoveal, temporal and nasal choroidal thicknesses were measured as 351.90 µm±103, 335.10±100 µm, 322.00±99 µm, respectively in the ocular rosacea group; as 323.50±61 µm, 311.95±63, 302.35±61 µm, respectively in the control group. However, all these differences were not found to be statistically significant ($p>0.05$).

Conclusion: Though many vascular disorders are observed in ocular rosacea, choroidal thickness is not affected by them. New studies including more patients with a longer period of follow-up are needed in this field.

Introduction

Rosacea is a chronic inflammatory dermatological disease characterized with erythema, telangiectasias, papules and pustules that is seen more frequently in individuals with fair skin [1]. It is usually diagnosed between the ages of 40-59, however the disease can be seen in all age groups [2]. While the incidence of the disease in women and men is considered to be equal to each other, the rate of diagnosis in women is much higher [since hospital admission rates of women are higher] [3,4]. This disease has four subtypes such as erythematous telangiectasia, papulopustular, phymatous and ocular rosacea. Unlike other subtypes, phymatous rosacea is more common in men [3].

Ocular rosacea is bilateral disease with asymmetrical course; seen in 45% to 85% of rosacea patients, typically accompanied with erythematous telangiectasia on the edges of the eyelids and Meibomian gland disease [1,3]. Ocular irritation, itching, redness, photophobia, epiphora and amblyopia due to cornea involvement are the main symnptoms of the disease [4].

In the diagnosis of rosacea and ocular rosacea, criteria determined with Rosasea Consensus panel (ROSCO) are used [5]. However, making a diagnosis might be difficult since these signs and findings are not specific to the disease. Though the accurate etiology of the disease remains uncertain, triggering factors such as sun and irritant agents resulting in endothelium dysfunction are thought to initiate the disease [6]. Immune system and vascular system abnormalities, genetic factors, Helicobacter pylori and some infections like demodex are other factors that are considered to be responsible for the pathophysiology [7-10].

Interleukin 1 alpha and beta, matrix metalloproteinase (MMP) 8 and 9 among pro-inflammatory agents were found to be high in ocular rosacea patients [11,12]. Blushing of the face, erythema and telangiectasias seen in the disease are considered to be due to neurovascular response disorder [13]. Triggering factors such as Ultraviolet (UV) radiation, high temperature, spices trigger the release of inflammatory mediators and result in vasodilatation and erythema [14]. In skin biopsies of rosacea patients, vascular endothelial growth factor (VEGF) and VEGF receptors (VEGF-R1 and VEGF-R2) were determined to be high [15].

Though the disease is considered to be a localized one, some vasogenic diseases like hypertension and migraine were observed to be more frequent with rosacea [16,17].

*Corresponding author:
Email address: is_an89@hotmail.com (Isa An)

In recent years, evaluation of choroidal thickness with enhanced depth imaging (EDI) and optical coherent tomography (OCT) devices is especially considered to be a potential marker for inflammatory diseases having vascular component [18]. Some systemic and dermatological diseases with vascular etiologies were shown to impact choroidal sanguinolency in some studies [17,18].

In our study, we aimed to evaluate whether ocular rosacea disease with vascular etiology had impact on choroidal thickness. In addition, we aimed to evaluate whether central fovea thickness and retina nerve fiber layer (RNFL), or not.

Materials and Methods

In this prospective case-control study, right eyes of patients diagnosed with rosacea in the Dermatology Department of Şanlıurfa Training and Research Hospital between the years 2016-2020 who had ocular rosacea and had been monitored for at least a year were included. The ethics approval of the study was provided by the Ethics Committee of the Harran University Non Invasive Clinical Research (date:14.09.2020, number: HRU/20.16.14). Informed consents of participants were obtained and our study was designed in accordance with Helsinki Declaration.

According to ROSCO panel criteria, right eyes of thirty patients who had been diagnosed with ocular rosacea and followed-up for at least a year between the ages 25-60 and right eyes of same number of healthy individuals matched in accordance with age and sex were included in the study [5]. Patients having refractive error more the spherical equivalent of (SE) 3 diopters, patients with visual acuity less than 10/10, patients with axial length other than 21-24 mm, patients with history of ocular surgery and patients having additional ocular and systemic diseases other than rosacea were excluded from the study. Medical histories of all participants were obtained. All participants received full ophthalmological examination including best corrected visual acuity (BCVA), refraction examination, measurement of intraocular pressure (IOP), and examination of the anterior and posterior segments with biomicroscopy, measurement of axial length (AL). Central Fovea thicknesses, RNFL were automatically measured with OCT device (RS-3000, Nidek, Navis-Ex 1.5.5). The distance between two reference points of the choroidal layer (Bruch membrane and sclerochoroidal interface), was measured by the same person manually using a ruler found within the software of the device (Figure 1). Measurements were obtained from the central fovea, 1000 micron nasal and temporal to the fovea. In order to minimize diurnal fluctuations in the choroidal thickness, measurements were performed within the same time intervals (13.30-16.00).

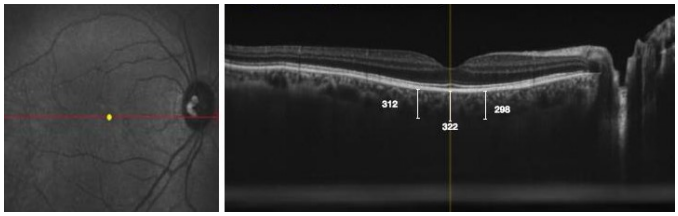

Figure 1. The distance between two reference points of the choroidal layer (Bruch membrane and sclerochoroidal interface).

Statistical analysis

Considering the comparison of foveal thickness and RNFL values between the two groups by using Independent sample T test, The effect sizes for choroidal thickness values (mean ± SD) of two groups were determined as between 0.324 and 0.371, by using G-power 1.3.9.4. version software. The powers of these analyses were calculated as between 0.847 and 0.892. Statistical analysis of data were performed by using SPSS program. (IBM statistics for Windows version 25, IBM Corporation, Armonk, New York, USA, License: Harran University). Continuous data was presented as mean ±SD, whereas categorical data as number of cases and percentage. Chi-square test was used in the comparison of gender distribution. Kolmogorov-Smirnov test, histogram and Q-Q plot graphics were used to determine if data show normal distribution. Mann-Whitney U test were used for comparisons of nonparametric data including choroidal thickness values. A p value less than 0.05 was considered to be statistically significant.

Results

Thirty patients diagnosed with ocular rosacea and 30 healthy individuals matched in accordance with age and sex were included in the study. Average age was calculated to be 42.06±13 (female/male ratio - 20/10) in ocular rosacea patients, and as 41.90±14 (female/male ratio-20/10) in control group participants. When age, sex, SE, AL and IOP were evaluated, significant difference was not detected between these two groups ($p>0.05$) (Table 1). Mean central, temporal and nasal choroidal thicknesses were calculated to be 351.90±103 µm, 335.10±103 µm, 322.00±99 µm in the rosaceae group, respectively; and as 323.50±61 µm, 311.96±63 µm, 302.36±61 µm, respectively in the control group. Significant difference was not detected between the groups in respect to central, temporal and nasal choroidal thicknesses ($p>0.05$) (Table 2). Fovea thicknesses were calculated to be 222.90±19 µm on the average in rosacea group and as 228.75±9 µm on the average in control group. Mean RNFL was found to be 108.00±9 µm in rosacea group, and 105.05±8 µm in control group. Mean fovea thicknesses and mean RNFL thicknesses were similar between the groups ($p>0.05$).

Discussion

Choroid layer is a highly vascularized tissue that provides blood to the retina layer of the eye. Choroidal tissue was demonstrated to be affected by many systemic diseases having vascular etiology in various studies [18-20]. Evaluation of the choroidal layer with OCT devices may provide important data related to some diseases. Non-invasive nature of the device and administration of it within a short period of time are important advantages [19,20]. Neurovascular regulation disorder has an important role in the patophysiology of rosacea disease [13]. In previous studies, triggers such as spicy foods, UV radiation and

Table 1. Demographic properties of groups.

Demographic properties of groups	Rosacea	Control	p values
Eye, n	30	30	
Age, mean ± SD (years)	42.05 ± 13.30 (min-20, max-62)	41.90 ± 14.05 (min-21, max-65)	0.963
Sex (male/female ratio), n	10/20	10/20	1

SD: Standard deviation, Min: minimum, Max: maximum.

Table 2. Choroidal thicknesses of the patients and the th control group; RNFL and fovea thicknesses.

Demographic properties of groups	Rosacea mean ± SD (µm) (min-max)	Controlmean ± SD (µm) (min-max)	p values-t test
Subfoveal choroidal thickness	351.90 ± 103 (82-512)	323.50 ± 61 (201-418)	0.202
Temporal choroidal thickness	335.10 ± 100 (89-496)	311.96 ± 63 (192-416)	0.292
Nasal choroidal thickness	322.00 ± 99 (78-482)	302.36 ± 61 micron (189-401)	0.361
Central foveal thickness	222.90 ± 19 (150-263)	228.75 ± 9 (209-247)	0.146
RNFL	108.00 ±9 (91-130)	105.03 ±8 (87-120)	0.191

SD: Standard deviation, Min: minimum, Max: maximum, RNFL: Retinal nerve fiber layer.

high temperature were shown to increase the release of inflammatory mediators by resulting in vasodilatation, erythema and redness via a mechanism involving temporary receptor potential vanilloid (TRPV) cation channel family [21]. TRPV was found to increase in skin biopsies of rosacea patients [21]. Moreover, VEGF and VEGF receptors having important roles in the neurovascularization cascade were determined to be higher than normal amount in rosacea patients [15]. The most important finding of ocular rosacea is the clustering of telegiectatic veins at the edges of the eyelids, which is a vascular finding. Definite information about whether neurovascular dysregulation in the pathogenesis of rosacea also affects the choroid layer, or not is not yet present. In our study, we compared choroidal thicknesses of rosacea patients having ocular involvement with healthy control group matched in respect to age-sex. According to ROSCO classification, 26 patients having mild rosacea (mild blepharitis and eyelid edge telangiectasias), 2 patients with mild-to-moderate (blepharoconjunctivitis) and 2 patients with moderate-to-severe (blepharokeratoconjunctivitis) ocular rosacea were present5. None of our patients had severe (sclerokeratitis-anterior uveitis) ocular involvement. When we analyzed the data, we observed that choroidal thicknesses of ocular rosacea group were 28 µm thicker at the subfoveal region, 24 µm thicker at the temporal region and 20 µm thicker at the nasal region compared to control group. However, these differences were not found to be statistically significant in our study ($p > 0.05$). Dermatological disease have been the focus of interest recently in respec to choroidal thickness examination. Akkurt et al., found that ocular sanguinolency increased in psoriasis patient [22]. Türkçü et al., found that choroidal thickness was high in psoriasis patients [23]. Ersan et al., and Aksoy et al., found that subfoveal choroid layer was thicker in severe psoriasis patients [19,24]. Aksoy et al., Korkmaz et al., found RNFL to be thinner compared to healthy control group [24]. However, Şahin et al., Kılıç et al., reported that choroidal thickness and RNFL were similar with the control group [25,26]. Öncül et al., and Fouad et al., Demirkan et al., detected lower choroidal thickness in vitiligo patients [27-29]. Özlü et al., examined choroidal thickness in lichen planus patients and reported that choroid layer was thinner in these patients [30]. In the literature, a study on the measurement of choroidal thickness in rosacea disease is present [31]. Şahin et al. [31] compared 42 papulopustular and 38 erythema telangiectasia rosacea patients with 37 healthy participants. Subfoveal central choroidal thicknesses were found to be 352 µm in papulopustular group, as 331 µm in erythema telangiectasia and as 346 µm in control group. These data were not found to be statistically significant. It was interpreted that choroid layer was not affected in rosacea disease. In this study, Heidelberg OCT device was used unlike our study. In the literature, eye involvement ratios of rosacea patients varied between 45% and 85% [3,5,16].

In the study by Şahin et al. [31] eye involvement ratios were not specified. In our study, we only included patients having eye involvement different than their study. However, we still could not detect a statistically significant difference. Our study had some limitations. First of all, age group of our patients was homogenous. Our patient numbers were not sufficient to perform sub-group analyses. In rosacea patients, central subfoveal choroidal thickness interval was (82 µm -512 µm) much higher than the control group (201 µm -418 µm). We believe that this finding can be clarified with studies having longer follow-up periods performed with a bigger patient group in which changes in choroidal thickness in time can be analyzed. Furthermore, we think that studies performed with a narrower age group might yield more clarifying results.

Finally, we believe that evaluations performed with OCT-angiography device providing more detailed information related to the structure of choroidal venation would provide additional benefit for the studies in this field.

Conclusion

As a result, we determined that mean choroidal thicknesses of ocular rosacea patients were similar to health individuals. Studies including higher number of participants and having longer follow-up periods are required in this field.

Highlight key points

- Ocular rosacea is bilateral disease with asymmetrical course; seen in 45% to 85% of rosacea patients.
- Some dermatological diseases with vascular etiologies were shown to impact choroidal sanguinolency in some studies.
- Though many vascular disorders are observed in ocular rosacea, choroidal thickness is not effected by them.

Ethical approval

The ethics approval of the study was provided by the Ethics Committee of the Harran University Non Invasive Clinical Research (date:14.09.2020, number: HRU/20.16.14).

Conflicts of interest

There are no conflicts of interest.

Financial support

There is no financial support.

Data availability statement

No data are available.

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