OCT-A Changes in Patients with Hemoglobinopathy

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Research Article

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Abstract

Purpose: The aim of this study is to evaluate retinal vascular changes in patients with sickle cell disease and thalassemia with optical coherence tomography angiography (OCT-A).

Methods: For this purpose, 98 patients with sickle cell disease, 75 patients with beta-thalassemia and 100 healthy control groups in Mersin University Hospital between January 1, 2020 and November 1, 2021 were included in this study. OCT-A imaging was performed with ZEISS AngioPlex OCT angiography (Carl Zeiss Meditec, Dublin, CA, USA).

Results: All OCT-A parameters (FAZ area, circularity, perimeter, vessel and perfusion density) were found to be statistically significantly different in both patients with thalassemia and patients with sickle cell disease when compared to healthy controls.

Conclusion: In conclusion, retinopathy that may occur in patients in both hemoglobinopathy subgroups can be diagnosed and followed up with OCT-A. It has also been found that OCT-A parameters are affected even before clinically detectable retinopathy develops.

Introduction

Hemoglobinopathies, the most common hereditary blood disease in the world, are caused by structural changes or synthesis disorders in the polypeptide chains of the hemoglobin molecule. They are divided into two main classes, abnormal hemoglobins and thalassemias. Sickle cell disease is a group of inherited hematological diseases in which erythrocytes characteristically distort the biconcave disc shape and take a sickle shape. This situation causes vasoocclusion and can affect all organs [1].

The most common causes of vision loss in patients with sickle cell disease are proliferative sickle cell retinopathy (PSCR) characterized by chronic peripheral retinal microvascular occlusion and ischemia [2]. Retinopathy due to sickle cell disease is divided into proliferative and non-proliferative. The grade of proliferative retinopathy is determined by the Goldberg classification (Table 1) [3].

Thalassemia is a genetic blood disease characterized by a decrease or complete absence in the synthesis of one or more of the globin chains in the structure of the hemoglobin molecule. It is classified according to the reduced or non-synthesized globin chain. The best described types are α and β thalassemia [4].

The frequency of eye involvement in β-thalassemia was found to be 41,3–85% in various studies [5]. Patients suffering from β-thalassemia major and minor can develop two different kinds of retinal abnormalities which are pseudoxanthoma elasticum-like retinal abnormalities and non-pseudo-xanthoma elasticum-like retinal abnormalities. Pseudoxanthoma elasticum-like (PXE-like) lesions include angioid streaks and optic disc drusen. Angioid streaks are characterized by irregular breaks in the Bruch's membrane. Although characteristically asymptomatic, they may lead to visual symptoms if they involve the macula or are complicated by neovascularization. Non-pseudoxanthoma elasticum-like (Non PXE-like) abnormalities, causing retinal pigment epithelium degeneration and atrophy [6].

Materials-methods

Ethical permissions required for this study were obtained from Mersin University Clinical Research Ethics Committee. Written informed consent forms were obtained from all subjects included in this study, and this study was conducted in accordance with the Declaration of Helsinki. Patients who underwent OCT-A (ZEISS AngioPlex OCT angiography, Carl Zeiss Meditec, Dublin, CA, USA) imaging due to beta-thalassemia or sickle cell disease between 01/Jan/2020 and 01/Nov/2021 in Department of Ophthalmology, Faculty of Medicine, Mersin University were included in this study.

Demographic data, hemoglobin values and OCT-A parameters of the patients included in this study were evaluated. The foveal avascular zone (FAZ) area (in square millimeters) is the area of the capillary-free zone within the macular region surrounded by interconnected capillary beds and the FAZ perimeter (in millimeters) is the length of the boundary demarcating the FAZ. FAZ circularity (unitless) quantifies how close the shape of the FAZ is to a perfect circle, with a value of 1,0 denoting a perfect circle. Vessel density (in millimeters per square millimeter) is defined as the total length of perfused vasculature per unit area in the region of measurement whereas perfusion density (%) is the area occupied by the perfused vasculature per unit area in a region of measurement. The perfusion density and vessel density for the central 1-mm macula zone (equivalent to the Early Treatment Diabetic Retinopathy Study [ETDRS] central foveal ring) of the OCT-A images were analyzed.

Low-quality scans were excluded, and the procedure was repeated until good-quality scans were achieved. To image the FAZ region, a foveal-centered scan area of 3 × 3 mm was chosen. Statistical analysis of study data was done with SPSS 23.0 package program. Number and percentage were used for categorical variables. For continuous variables, it is shown as mean ± standard deviation. The conformity of continuous variables to the normal distribution was checked using the Shapiro-Wilk test. Student's t-test was used to compare the means of two independent groups, and ANOVA was used to compare the means of more than two independent groups. The chi-square test was used to compare categorical variables. Statistical significance level was taken as $p < 0.05$ for all comparisons.

Results

One hundred healthy controls, 98 patients with sickle cell disease and 75 patients with beta thalassemia were included in this study. The age and gender distributions of all participants are summarized in Table 2, and no statistically significant difference was found between them.

Of the patients with sickle cell disease, 31 (31,6%) were homozygous and 67 (68,4%) were heterozygous. In addition, retinopathy was not detected in 61 (62,2%) patients, non-proliferative sickle cell retinopathy (NPSCR) was found in 20 (20,4%) patients, and proliferative sickle cell retinopathy (PSCR) was found in 17 (17,4%) patients. The distribution of retinopathy in sickle cell patients is shown in Table 3.

The OCT-A parameters and hemoglobin levels of all participants are explained in Table 4. All parameters (FAZ area, circularity, perimeter, vessel and perfusion density) for all three groups showed statistically significant differences between the groups (for all parameters, $p < 0,05$).

When the hemoglobin levels of the all patients and their OCT-A parameters were compared, a statistically significant correlation was found in all parameters in patients with beta-thalassemia major, while no statistically significant correlation was found in any parameter in patients with sickle cell disease (Table 5).

When the subgroups of the diseases were compared with the control patients, the difference between the measurements of the patients with thalassemia major and homozygous-sickle cell disease was found to be statistically significant (for all parameters, $p < 0,05$). In addition, no statistically significant difference was found between the measurements of patients with sickle cell disease but without retinopathy and the control group (for all remaining parameters except vessel density, $p > 0,05$), (for vessel density $p = 0,038$, $p < 0,05$)

Discussion

Retinal hypoxia, ischemia, and neovascularization may develop after microvascular occlusion seen in patients with sickle cell disease. Neovascularization that occurs before the development of vitreous hemorrhage or retinal detachment is the most important precursor [7].

In different studies, retinal disorders such as retinal pigment epithelial degeneration and mottling, peripheral and central retinal thinning, venous tortuosity, retinal hemorrhage, retinal edema, cup-to-disk ratio enlargement and macular scarring have been reported in beta-thalassemia patients. The prevalence of reported retinal disorders differs between studies [8].

The main aim of this study is to evaluate the retinal changes that may occur in patients with hemoglobinopathy with OCT-A. There are statistically significant differences in angiography parameters between patients with hemoglobinopathy and healthy controls.

Lynch et al, included fifty-two patients with SCR (33 non-proliferative and 19 proliferative) and 20 healthy controls in their study. FAZ perimeter and acircularity index were significantly higher in SCR eyes compared to controls. In addition, vessel density in SCR eyes was significantly lower than in the control group [9].

Zhou et al included 31 patients with SCR (21 NP-SCR and 10 P-SCR) and 14 healthy controls in their study. All FAZ (area, perimeter, acircularity) measurements were significantly higher in NP-SCR and P-SCR subjects than in healthy controls [10].

Han et al., in their study including 82 eyes of 46 patients, found that there was a loss of flow and a decrease in vessel density in patients with sickle cell retinopathy [11].

In a study published in 2018, 36 eyes of 19 patients were evaluated. The mean ischemic index was found to be higher in patients with sickle SC (8,0%) than in patients with sickle SS (3,2%; $p = 0.01$). The ischemic index was also higher in patients with proliferative sickle cell retinopathy (9,3%) than in those without (2,8%; $p < 0.01$) [12].

This is the largest study using OCT-A imaging in patients with beta-thalassemia and sickle cell disease reported in the literature. However, by using different imaging devices, the accuracy of imaging protocols that have not yet been standardized can be increased.

In conclusion, it was determined that all FAZ parameters (area, circularity, perimeter) were significantly different in patients with both beta-thalassemia and sickle cell disease, even if retinopathy was not clinically developed. In addition, vessel and perfusion density were found to be lower in both patient groups compared to healthy controls. However, no significant correlation was found between the severity of retinopathy of the patients and angiography parameters. In addition, a correlation was observed between hemoglobin levels and angiography parameters in patients with beta-thalassemia major.

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Tables

Tables 1 to 5 are available in the Supplementary Files section.

Supplementary Files

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