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Original Article

Subfoveal Choroidal Thickness and Ganglion Cell Complex in Children with Type 1 Diabetes Mellitus Without Diabetic Retinopathy

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Abstract

Objectives: This study is an analysis of the subfoveal choroidal thickness (SFCT) and ganglion cell complex (GCC) in children who have type 1 diabetes mellitus (T1D) without diabetic retinopathy.

Methods: In all, 36 right eyes of 36 patients with T1D and 36 right eyes of sex- and age-matched healthy subjects were included in this prospective study. SFCT and GCC measurements were obtained using spectral domain optical coherence tomography (SD-OCT). Correlations between SCFT, GCC and duration of T1D, glycated hemoglobin, and age were also investigated.

Results: The mean SFCT was 342.1±42.3 μm in the T1D group and 354±70.8 μm in the control group (p>0.05). There was no significant difference between the groups in the GCC superior and inferior retina values. The average GCC was thinner in the T1D group (T1D group: 88.11±14.93 μm, control group: 103.39±15.65 μm; p=0.005). The mean central retinal thickness (CRT) was decreased in the T1D group (T1D group: 248.1±16.5 μm, control group: 262.1±18.3 μm; p=0.021).

Conclusion: The mean SFCT was not significantly different in diabetic children compared with healthy eyes. The CRT and average GCC thickness were lower in children with T1D. SD-OCT can reveal neurodegenerative changes that may occur before vascular changes in diabetic children.

Keywords: Choroidal thickness, ganglion cell complex, type 1 diabetes mellitus.

Introduction

Diabetes mellitus (DM) is the third most common chronic disease in childhood and the majority of children with diabetes have type 1 diabetes (T1D) (1–3). There are numerous studies about diabetic retinopathy (DR), which can cause vision loss (4, 5). Yet despite significant DR research, there are few studies of choroidal vasculopathy in diabetic children. The choroid layer is located between the sclera and the retinal pigment epithelium (6). The vascularized structure of the choroid accounts for 85% of total ocular blood flow. Outer retinal layers are provided with oxygen by the choroid (7). Some studies have shown that choroidal pathologies, such as aneurysms, obstruction of the choriocapillaris, and vascular degeneration, have a role in the pathogenesis of DR (8–10). Measurement of subfoveal choroidal thickness (SFCT) is considered a means of assessment of choroidal blood flow. There are many studies with conflicting findings about choroidal thickness in diabetic patients (11–13). The precise relationship between choroidal thickness and DR remains unresolved.

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Various studies have reported neural tissue loss, such as ganglion cell complex (GCC) neural cells in the retina, occurring before a clinical presentation of DR (14–17). Therefore, early detection of GCC loss and choroidal vasculopathy in T1D patients may be useful to prevent the development of DR.

The aim of the current study was to analyze the SFCT and GCC in children with T1D without DR.

Methods

This prospective, comparative study was performed at the University of Health Sciences Okmeydanı Research and Training Hospital. The research was approved by the ethics committee and the tenets of the Declaration of the Helsinki were observed (09.2018.120). Written, informed consent was obtained from the parents of all of the patients.

In all, 36 right eyes of children with T1D and 36 eyes of sex-and age-matched healthy control subjects was enrolled in the study. All of the participants underwent a complete ophthalmic examination: Best-corrected visual acuity (BCVA) evaluation, slit lamp examination, intraocular pressure (IOP) measurements with a pneumotonometer, fundus examination, and refraction measurements with an auto kerato-refractometer were performed. Refraction measurements and the fundus examination were performed after attaining cycloplegia. The duration of DM, age, gender, and glycated hemoglobin (HbA1c) level data of the diabetic group were recorded. The duration of T1D was at least 1 year in the patients enrolled in the study and all used insulin. Patients >18 years of age, contact lens users, those with a previous ocular trauma, history of ocular surgery, ocular inflammation, refractive errors > ±1.00 diopters (D) (spherical or cylindrical), axial length >26.00 mm or <22.00 mm, corneal disease, or cataract were excluded from the study.

All of the OCT images were obtained using a spectral domain OCT instrument (Spectralis; Heidelberg Engineering, Heidelberg, Germany). During the follow-up period, the eyes were scanned using the eye-tracking-based follow-up function of the Spectralis platform. The SFCT was evaluated using enhanced-depth imaging OCT (EDI-OCT). GCC thickness was defined as the distance from the internal limiting membrane to the outer boundary of the inner plexiform layer and the value was calculated automatically by the OCT device. The eye was divided into 2 sectors: superior and inferior. The GCC was expressed as the average thickness of the all sectors (AvgGCC) and separate values for the superior (SupGCC) and inferior (InfGCC) sectors. The central retinal thickness (CRT) was calculated automatically as the distance between the inner limiting membrane and the retinal pigment epithelium-choriocapillaris interface of the radial lines through the foveal area. All of the measurements were performed between 9:00 am and 12:00 pm to avoid diurnal variations.

The statistical analyses were performed using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA). Descriptive analyses are presented using mean and SD for normally distributed variables. An assessment of normality was performed using the Kolmogorov-Smirnov test. The independent-t test, Student t-test, and Pearson correlation test were applied. A p value of <0.05 was considered a statistically significant result.

Results

The female/male ratio was 20/16 in both groups. The mean age was 15.33±2.16 years in the T1D group and 15.28±1.67 years in the healthy group. There was no significant difference between the groups in terms of age and sex. The mean duration of diabetes mellitus was 4.5±3.5 years. The mean HbA1c level was 9.4%±1.8% (minimum 6%, maximum 14%). The groups did not differ significantly in BCVA or IOP. The baseline characteristics of the subjects are shown in Table 1. The mean SFCT was 342.1±42.3 μm in the T1D group and 354±70.8 μm in the control group (p>0.05) (Fig. 1). There was no significant difference between the groups in the GCC superior and inferior retina. The AvgGCC was lower in the T1D group (p=0.005). There was no significant correlation between GCC thickness and HbA1c, duration of DM, or age. The results of GCC measurements are displayed in Table 2. The mean central retinal thickness (CRT) was lower in the T1D group (T1D group: 248.1±16.5 μm, control group: 262.1±18.3 μm; p=0.021).

Table 1. The baseline characteristics of the subjects

Variable	T1D group	Control group	p
Eyes (N)	36	36	
Gender			
Female	20	20	0.505
Male	16	16	
Age (years)	15.33±2.16	15.28±1.67	0.932
Spheric equivalent	0.08±1.35	0.11±1.33	0.951
Axial length	22.47±1.18	22.29±0.90	0.612
IOP	16.33±2.44	16.11±1.93	0.765
BCVA	20/20	20/20	
HbA1c	9.4%±1.8%		
DM duration	4.5±3.5 years		

BCVA: Best-corrected visual acuity; DM: Diabetes mellitus; HbA1c: Glycated hemoglobin; IOP: Intraocular pressure; T1D: Type 1 diabetes mellitus.

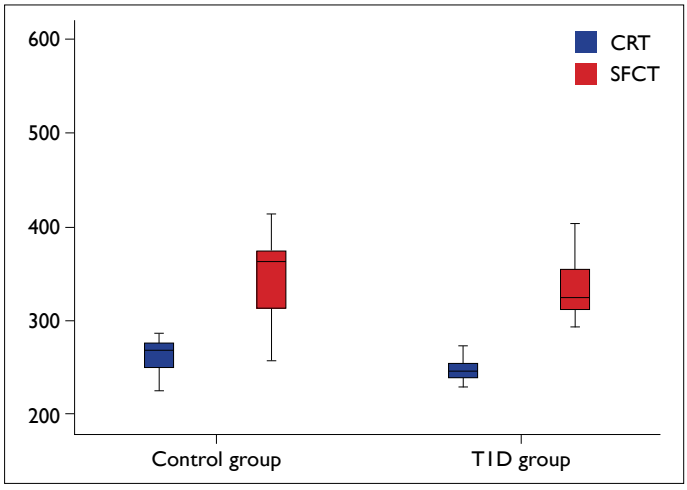

Figure 1. Subfoveal choroidal thickness (SFCT) and central retinal thickness (CRT) of the subjects.

Table 2. Ganglion cell complex (GCC) measurements of the subjects

Variable	T1D group	Control group	p
AvgGCC (µm)	88.11±14.93	103.39±15.65	0.005
SupGCC (µm)	100.33±22.81	109.89±8.79	0.112
InfGCC (µm)	95.33±22.97	105.11±7.20	0.094

AvgGCC: Average GCC; InfGCC: Inferior GCC; SupGCC: Superior GCC.

Discussion

The choroid, the vascular layer of the eye, is involved in the pathophysiology of DR. Loss of the choriocapillaris has been demonstrated in patients with DM in histopathological studies. This loss results in reduced choroidal blood flow, and can lead to photoreceptor disfunction and retinal hypoxia (8–10). Querques et al. (18) investigated changes in macular choroidal thickness in patients with various stages of DR. They found that the choroidal thickness was lower in the diabetic patients compared with healthy patients, regardless of DR stage. They also reported that the SFCT was not significantly different between diabetic patients with DR and without DR. In contrast, Sheth et al. (19) found a significant reduction in choroidal thickness in patients with ischemic diabetic maculopathy compared with nonischemic DR and diabetic patients without DR. Our results revealed no significant difference between groups. Vujosevic et al. (20) found no significant difference in choroidal thickness between diabetic patients with or without DR and healthy subjects. However, the cited studies examined adulthood DM. Sayin et al. (21) and Golebieska et al. (15) observed no significant difference between groups in diabetic children. Their findings support our result. The effects of DM on choroidal thickness in childhood appear to differ from what has been seen in adulthood. Many factors may influence choroidal thickness, such as age, gender, refractive error, and longer axial length (22–25). There was no significant difference in these factors between groups in our study. These children need more follow-up to assess the clinical significance of these findings and to determine the potential impact on DR onset.

The pathophysiology of retinal neurodegeneration is not yet fully understood. Ocular and systemic factors involved include increased inflammation and oxidative stress, loss of neuroprotective factors, hyperglycemia, dyslipidemia, insulin deficiency, and glutamate excitotoxicity (26, 27). Previous studies have found that retinal neurodegeneration is one of the earliest detectable changes in patients with DM (28-30). Our study results demonstrated a significant reduction in the average GCC thickness in children with T1D compared with healthy subjects. El-Fayoumi et al. (31) had similar results. In their study, the GCC and RFNL thickness in children with T1D was significantly lower. As we did, they found no correlation between GCC thickness and HbA1c, duration of DM, or age. Golebiewska et al. (15) did not observe any difference in GCC thickness in T1D children, but they reported a significant difference in GCC focal loss volume. Pierro et al. (32) found a decreased GCC and choroidal thickness in patients with type 2 DM, but not in T1D. They suggested that insulin resistance might be a cause of neurodegeneration.

The primary limitations of our research are the small sample size and the single-center study design.

In conclusion, SFCT did not change in children with T1D; however, GCC thickness was decreased in T1D. OCT can reveal early changes in neuroretinal tissue. Multicenter studies and a larger sample as well as extended follow-up data are needed to determine whether these findings are predictive factors of DR in children.

Disclosures

Ethics Committee Approval: Ethic Committee of Marmara University, protocol number 09.2018.120.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Involved in design and conduct of the study (AHB, DB); preparation and review of the study (AHB, AC, ME); data collection (AHB, DB); and statistical analysis (AHB, AC, ME).

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