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Central corneal thickness in children with type 1 diabetes mellitus and the effect of metabolic control on corneal thickness

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ABSTRACT

Objective: To research whether central corneal thickness (CCT) of children with Type 1 diabetes mellitus (T1D) is different from healthy children at same age group and whether metabolic control has an effect on corneal thickness.

Materials and methods: The children with T1D who applied to our outpatient department with the aim of controlling for possible diabetes complications and who had no diabetic retinopathy were prospectively evaluated. The healthy children from the same age group who applied to our outpatient setting for eye control and who had no systemic or eye disease were included in the control group. The CCT of all children was measured with ultrasonic pachymeter with topical anesthesia.

Findings: While the corneal thickness for healthy children was 554.25±42.85 (500 – 678 µ), the average corneal thickness for diabetic children was 567.38±33.28 (487 – 628 µ). A significant difference was detected for average corneal thickness (Z=-2.040 p=0.041). No relation was detected between the central cornea thickness and the duration of diabetes (t=1.418 p=0.168), average HbA1C level (t=1.261p=0.218), hyperglycemia (t=0.228 p=0.821) and hypoglycemia attack number (t=-0.332 p=0.743).

Result: CCT is increased in the patients compared to the control group even before diabetes mellitus (DM) has developed a retinopathy. A relation of this increase with period of diabetes, HbA1C level and hypoglycemia attack number could not be detected.

Key words: *Central corneal thickness, type 1 diabetes mellitus*

Introduction

Diabetes mellitus (DM) may lead to some ischemic conditions such as coronary artery disease, peripheral artery disease and retinopathy. It is characterized by a hyperglycemia that may cause microvascular and/or macrovascular complications over time. Although diabetic retinopathy is its most common complication and neovascular glaucoma, refractive changes[1] and various corneal disorders may be also seen. These include dysfunction in the corneal endothelium, desensitization[2], stromal and subbasal nerve abnormalities[3], low endothelial density and hexagonality[4], increased corneal autofluorescence[5], fragility that is raised with the decrease in corneal sensitivity, recurrent epithelial erosions, epithelial edema, desensitization and neurotrophic ulcers. Following argon laser iridotomy and intraocular surgery, endothelial dysfunction and persistent stromal edema were the other corneal disorders

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that we were found in DM patients[6, 7]. It was noticed in many publications[8-16] that central corneal thickness (CCT) is increased in adult diabetes mellitus patients. However, this increase was not observed in some of the studies, [17-19]. In the studies that were done on the children with T1D, it was detected that in general CCT was increased compared to the healthy children group[20,21]. In our study, we aimed to measure the CCT of children with T1D and to research whether these values were related to the duration of diabetes, HbA1C level and the hypoglycemia attack numbers.

Materials and Methods

Forty-nine children with Type 1 diabetes mellitus who came to our outpatient department with the aim of controlling for possible diabetes complications and who had not retinopathy finding and 46 children in the same age group who came to our outpatient setting for eye examination (control group) were included in this study. The children who had systematic diseases except for DM and who had been receiving a topical or systematic treatment were not included in the study. At the same time, the ones who had eye surgery history, who had been using contact lens and who were glaucoma or uveitis patients and had cornea pathology were not included in the study. After the complaints and histories of all patients were taken, visual acuity, intraocular pressure measurement (IOP), biomicroscopy and fundus examinations were carried out. CCT of all patients was measured with ultrasonic pachymeter device (opticon pacline) with topical anesthesia. The measurements were done by the same person and after 3 measurements were taken for each eye, the values were averaged and recorded. The ones who were outside of the -2,00 D to +2,00 D interval of refractive errors were not included in the study. SPSS (statistical package for the social sciences) for Windows 18 package program was used for the statistical analysis and conformity of the data with a normal distribution was controlled by the Kolmogrov-Smirnov test. Mann-Whitney U test, independent sample t-test, Chi-square test and Pearson correlation analysis as well as definitive statistical methods and frequency distributions were used in the analysis and $p<0.05$ values were considered as statistically significant.

Results

The age average for diabetic children was 12.48 ± 3.47 (5 – 17 years), while the age average for the control group was 11.58 ± 2.23 (5 – 16 years). The gender distribution for diabetic children was 23 (44.8%) males and 26 (55.2%) females, while the gender distribution for control group was 25 (57.7%) males and 21 (42.3%) females. There was no significant difference between the groups in terms of gender distribution ($\chi2=0.908$ $p=0.341$) and age average ($t=1.136$ $p=0.261$). The cornea thickness was 567.38 ± 33.28 (487 – 628 μ) in diabetic children and 554.25 ± 42.85 (500 – 678 μ) in the control group (Table 1). There was a significant difference between the groups in terms of cornea thickness ($Z=-2.040$ $p=0.041$). The average duration of diabetes in diabetic children was 4.72 ± 2.26 years (1 – 9, median 4 years), HbA1C level was 8.14 ± 2.21 (4 – 13, median 8), hyperglycemic attack number was 3.41 ± 2.73 (0 – 14, median 3 times) and hypoglycemic attack number was 0.24 ± 0.43 (0 – 1 time). When a comparison was done according to the duration of diabetes (median 4 years), while the cornea thickness was 556.36 ± 45.08 μ in children whose period of diabetes was <4 years, the cornea thickness was 574.11 ± 22.44 μ in children whose period of diabetes was ≥4 years and the difference is not statistically significant ($t=1.418$ $p=0.168$). No correlation between the diabetes period and cornea thickness was observed ($r=0.185$ $p=0.336$). When a comparison was done according to the HbA1C level (median 8), the cornea thickness at children <8 was 556.75 ± 14.11 μ and the cornea thickness at children ≥ 8 was 572.97 ± 25.14

Table 1. Age, gender and cornea thickness correlation.

		Gender		
	Age (mean value)	Male	Female	Cornea thickness (μ)
Diabetic children	12,48 ± 3,47	23	26	567,38 ± 33,28
Control	11,58 ± 2,23	25	21	554,25 ± 42,85

Table 2. HbA_1C value, hyperglycemic attacks number and cornea thickness correlation.

		Cornea thickness (μ)
HbA_1C value	<8	556,75 ± 14,11
	>8	572,97 ± 25,14
Hypergycemic attacks number	<3	565,89 ± 11,48
	>3	568,77 ± 22,28

μ (Table 2); the difference between the cornea thicknesses according to HbA1C level was not significant (t=1.261 p=0.218). A correlation between HbA1C and cornea thickness was not observed (r=0.140 p=0.469). In the comparison done according to the hyperglycemic attack number (median 3), the cornea thickness in the children who had <3 attacks was 565.89 ± 11.48 μ and the cornea thickness at the children who had ≥3 attacks was 568.77 ± 22.28 μ. There was no difference in terms of cornea thickness according to hyperglycemic attack number (t=0.228 p=0.821) (Table 2). A correlation between attack number and cornea thickness was not observed (r=-0.111 p=0.567). In the comparison of the ones who had hypoglycemic attack and had not hypoglycemic attack, the cornea thickness at the ones who had hypoglycemic attack was 571.20 ± 20.77 μ and the cornea thickness at the ones who had not hypoglycemic attack was 566.20 ± 36.71 μ. There was no difference between cornea thicknesses according to hypoglycemic attack number. A correlation between hypoglycemic attack and cornea thickness was not observed (r=0.06 p=0.743).

Discussion

Decreased corneal sensitivity, recurrent erosions, epithelial edema, Descemet's membrane wrinkles, neurotrophic ulcers and delayed wound healing are some of the pathologies that may occur in diabetic patients. It was shown that chronic metabolic stress occurring due to hyperglycemia may cause some morphological changes in the cornea endothelium but the studies on this topic are very limited[22]. There are several studies showing that there is a change in the corneal thickness of diabetic patients compared to normal individuals or not. Some of these were carried out only for T1D [2,10,20-22] and others were carried out for both T1D and type 2 DM (T2D) [4,8,17,23]. Although the cause of the changes that occur at level of the corneal thickness in diabetic patients remains uncertain, it is estimated that the pump function of the endothelium is impaired due to a Na+/K+ ATPaz activity disorder that results in stromal hydration[8,10,24]. McNamara et. al stated that hyperglycemia changed the cornea structure by impairing its hydration in diabetic patients and that accordingly the corneal thickness is also affected in these patients[25].

While Weston et. al [26] stated that endothelial permeability was decreased in diabetic corneas at different phases of hypoxia, Keoleian et. al [22] did not detected any difference in cornea thickness due to hypoxia.

There are also authors who explained the reason why the cornea thickness tends to increase in diabetic patients as a pleomorphism and polymegathism [10,27].

Schultz et. al stated that the endothelium cell density of T2D patients was not changed compared to the control group, that pleomorphism and polymegathism were increased and that the endothelium cell density was decreased in T1D [23]. It was brought forward that these changes may be due to the inadequacy of barriers and pump function in the cornea endothelium.

Roszkowska et. al explained that endothelial cell density was decreased in both T1D and T2D patients and pleomorphism and polymegathism was increased [8].

While Larsson et. al did not detect any change in T2D, pleomorphism and polymegathism was increased in T1D and corneal autofluorescence was not detected[17].

Inoue et al. stated that the endothelial cell density was decreased, the hexagonal cell percentage did not change and the variation coefficient was increased[19].

In our study, the endothelial cell was not studied. Tiutiuca detected in his study that CCT was significantly higher in diabetic children compared to normal children[20]. In the study that they did on adolescents and children, Urban et. al detected that CCT increased in the patient group compared to normal group and CCT could not be correlated with any systematic factor[21]. Also, Larsson et al.[17] and Keoleian[22] were not able to detect any relation between corneal thickness and high HbA1C level. Zengin et. al[28] detected that the CCT of adult patients who had higher HbA1C levels was thicker than the ones of patients whose HbA1C levels were lower. Although we de-

tected in our study that the CCT of T1D patients was significantly increased compared to healthy children, we could not detect any relation between CCT and the HbA1C level, period of diabetes or the hypo-hyperglycemic attack number.

In conclusion, it has been noticed in several studies that CCT is generally increased in the patients with both Type 1 and Type 2 diabetes mellitus[8-15,20,21] and our study supports those observations.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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