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The Influence of Type-1 Diabetes Mellitus on Central Corneal Thickness in Children

Tip-1 Diyabetes Mellitusun Çocuklarda Merkezi Kornea Kalınlığına Etkisi

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Summary

Objectives: To evaluate the central corneal thickness (CCT) in children with diabetes mellitus (DM), to compare the results with those of age- and sex-matched healthy subjects, and to assess the presence of any relationship between the disease-variable parameters and CCT.

Materials and Methods: This prospective, cross-sectional study included 138 eyes of 138 subjects. The CCT was measured by ultrasonic pachymetry in 66 children with type-1 DM and in 72 healthy subjects. The effects of the duration of DM, current hemoglobin A1c levels (HbA1c), and fasting blood glucose (FBG) levels on CCT were also evaluated.

Results: The demographic characteristics of the study and control groups were similar (p>0.05). The average CCT was greater in the study (555.2±38.6 µm) than in the control group (547.7±31.5 µm), but the difference was not statistically significant (independent t-test, p=0.211). CCT was also not significantly different in children with diabetes >5 years' duration (554.6±39.3 µm) compared to diabetes ≤5 years' duration (555.6±38.6 µm) (p>0.05), and there was no significant correlation between the CCT- and the DM-related parameters in the study group (p>0.05).

Conclusion: Our findings indicate that DM does not affect the corneal thickness in adolescents. We also did not find any significant correlation between disease-related variables and the CCT. (Turk J Ophthalmol 2014; 44: 445-8)

Key Words: Child, central corneal thickness, type-1 Diabetes Mellitus

Özet

Amaç: Bu çalışmada, merkezi kornea kalınlığının (MKK) Diyabetes Mellituslu (DM) çocuklarda ve yaş, cinsiyet eşleştirilmiş sağlıklı bireylerde karşılaştırılmasını ve hastalıkla ilişkili parametrelerin MKK ile olan ilişkisini araştırmayı amaçladık.

Gereç ve Yöntem: İleriye dönük, karşılaştırmalı çalışmaya 138 hastanın 138 gözü çalışmaya dahil edildi. MKK 66 tip-1 DM'li çocuk ve 72 sağlıklı bireyde ultrasonik pakimetri ile ölçüldü. Hastalık süresi, hemoglobin A1C (HbA1c) değeri, ve açlık kan şekeri (AKŞ) seviyesinin MKK üzerine olan etkisi araştırıldı.

Bulgular: Çalışma ve kontrol grubunun demografik özellikleri benzer idi (p>0,05). Ortalama MKK çalışma (555,2±38,6 µm) grubunda, kontrol (547,7±31,5 µm) grubuna göre daha yüksekti ancak bu fark istatistiksel olarak anlamlı değildi (bağımsız t-testi, p=0,211). MKK değeri, diyabet süresi >5 yıl olanlarda (554,6±39,3 µm), ≤5 yıl olanlara (555,6±38,6 µm) göre istatistiksel olarak anlamlı değildi (p<0,05). Aynı zamanda çalışma grubunda, MKK ile DM ilişkili parametreler arasında anlamlı bir korelasyon yok idi (p>0,05).

Sonuç: Bulgularımız DM'nin, çocuklarda kornea kalınlığını etkilemediğini göstermiştir. Ayrıca hastalıkla ilişkili parametreler ile MKK arasında herhangi anlamlı bir korelasyon yoktu. (Turk J Ophthalmol 2014; 44: 445-8)

Anahtar Kelimeler: Çocuk, merkezi kornea kalınlığı, tip-1 diyabetes mellitus

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Introduction

Diabetes mellitus (DM) is a systemic macro/microvascular disorder that causes various ocular problems. Previous studies have reported structural and functional ocular changes with DM such as increased corneal autofluorescence, decreased corneal sensitivity, impaired epithelial barrier function, abnormal corneal wound healing, endothelial pleomorphism and polymegathism and lower endothelial permeability.[1-6]

There are varying reports on central corneal thickness (CCT) changes due to DM.[6-12] To the best of our knowledge, there are only a few published studies on CCT in diabetic children.[13,14] The purpose of our study was to investigate whether there was a difference between the CCT of diabetic and healthy control children by using ultrasonic pachymetry and to evaluate the relationship between CCT measurements and diabetes mellitus-related variables including fasting blood glucose (FBG), hemoglobin A1c (HbA1c) level, and DM duration. We also evaluated the correlation between the CCT value and duration of diabetes by using a partial correlation coefficient after controlling for age.

Materials and Methods

This study included 66 patients with type-1 DM referred from the Endocrinology and Metabolism Clinic to the Ophthalmology Department, and 72 age- and sex-matched healthy subjects who had presented at the Ophthalmology Department for a routine ocular examination. All study procedures were conducted in accordance with the Declaration of Helsinki, and informed consent was obtained from the parents of all the participants. This study was approved by the Ethical Committee of the Ankara University School of Medicine.

None of the patients had glaucoma or had undergone laser treatment. Patients with a history of corneal disease, contact lens use, chronic use of topical ocular medications, ocular trauma or ocular surgery were excluded from the study. Healthy subjects who did not have a history of any systemic disease, family history of glaucoma or ocular problems other than refractive error were included as the control group.

Detailed ophthalmologic examinations were performed, including best-corrected visual acuities with Snellen charts, slit-lamp evaluation of anterior chamber examinations, and dilated fundus examination with a 78-D lens. Intraocular pressure (IOP) was measured with a Goldmann applanation tonometer. CCT was measured with the Tomey AL-1000 ultrasonic pachymeter (Tomey Corporation, Nagoya, Japan). The mean of 5 consecutive measurements was recorded. The duration of DM, the current HbA1c and FBG level, pubertal status, and accompanying autoimmune diseases were recorded in the study group. All the diabetic patients were divided into two subgroups according to the duration of diabetes: Subgroup A: ≤5 years, Subgroup B: >5 years.

For statistical analysis, Pearson correlation analysis was used to investigate the correlation between the right and left eye CCT and IOP values. The independent t-test was used to compare the differences regarding the CCT and IOP values between the two groups. We used a multivariate regression model to show the effects of the diabetes-related variables (duration of disease, HbA1c, fasting blood glucose level) on CCT. We also assessed the effects of diabetic duration on CCT by using a partial correlation coefficient to control for age. All the statistical analyses were carried out using the SPSS version 15.0 statistical analysis program. A p value <0.05 was considered statistically significant.

Results

We examined 66 patients with insulin-dependent diabetes in the study group, and 72 healthy subjects in the control group. The mean age was 13.1±3.5 years (7-22 years) in the study group, and 13.0±2.9 years (8-20 years) in the control group. There were 31 (47%) girls and 35 (53%) boys in the study group, and 43 (59.7%) girls and 29 (40.3%) boys in the control group. No significant differences were noted regarding age and gender between the two groups (independent t-test, p=0.846; chi-square test, p=0.133, respectively). The demographic characteristic of two groups are summarized in Table 1.

There was a high degree of correlation between the right and left eye IOP and CCT values of the groups (Pearson correlation test, r=0.813, p=0.0001 for IOP and r=0.965, p=0.0001 for CCT) and we therefore used the right eye values for statistical purposes.

In the study group, 9 (13.6%) children with diabetes mellitus had an autoimmune disease (Hashimoto's thyroiditis). Fifty-one (77.3%) patients were pubertal, and 15 (22.7%) were

Table 1. Demographic features of the groups

	Diabetic Group	Control Group	p value
No. Patients	66	72	
Age (years)	13.1±3.5 (7-22)	13.0±2.9 (8-20)	0.846*
Female/Male n (%)	31 (47%)/35 (53%)	43 (59.7%)/ 29 40.3%)	0.133**
Disease Duration (years)	5.1±3.4 (1-20)		

*: Independent t-test, **: Chi square test

Table 2. The mean CCT and IOP in the diabetics, control group and subgroups

	Study group	Control group	p value*	Subgroup A	Subgroup B	p value*
No. Patient	66	72		41	25	
Mean CCT	555.2±38.6	547.7±31.5	0.211	555.6±38.6	554.6±39.3	0.915
Mean IOP	15.7±4.0	15.2±3.1	0.394	16.9±3.6	15.3±2.5	0.320

*: Independent t-test, Subgroup A: The duration of diabetes mellitus was ≤5 years, Subgroup B: The duration of diabetes mellitus was >6 years

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prepubertal. The mean duration of diabetes was 5.1±3.4 years (1-20 years). None of the patients had diabetic retinopathy.

The mean CCT was 555.2±38.6 µm (442-651 µm) in the study group, and 547.7±31.5 µm (487-604 µm) in the control group. The mean CCT of subgroup B was 554.6±39.3 µm (484-628 µm), and subgroup A was 555.6±38.6 µm (442-651 µm) in the in the study group and the difference was not statistically significant (independent t-test, p=0.915). We also found no statistically significantly difference between CCT and duration of diabetes (r=0.004, p=0.978) using Spearman rho correlation coefficient test. The mean IOP value was 15.7±4.0 mm Hg (7.5-29.5 mm Hg) in the study group and 15.2±3.1mm Hg (9.0-21.5 mm Hg) in the control group and the difference between the two groups was not statistically significant (independent t-test, p=0.394). All our values are summarized in Table 2. A multivariate regression model indicated that disease-related variables (diabetes duration, Hemoglobin A1c and fasting blood glucose level), were not significantly correlated with central corneal thickness in the study group (Table 3).

Discussion

Diabetes mellitus is a common disease worldwide, and it is therefore necessary to investigate the relation between diabetes and central corneal thickness. CCT is an important parameter for the correct measurement of intraocular pressure (IOP) and clinical assessment of glaucoma as thick CCT values may cause falsely high IOP readings, and thin CCT values may cause falsely low IOP readings.[15-17]

Our data analysis showed that CCT was higher in children with diabetes mellitus than healthy control subjects but this was not statistically significant. None of the disease-related parameters (duration of diabetes, HgA1c, FBG) had any influence on CCT. There was also no statistically significant difference between the CCT values of diabetic children with diabetes for over 5 years and less than 5 years.

There are several other similar studies on the older diabetic patient. Wiemer et al.[18] found no statistical significantly difference in CCT measured with the Scheimpflug camera between the study group (102 patients with type 1 DM and 101 patients with type 2 DM) and healthy subjects (69 subjects) and the CCT was also not correlated with any systemic factors. Inoue et al.[19] evaluated the endothelial structure and thickness of the cornea in 99 eyes of type 2 diabetic patients. They found that corneal endothelial structure was damaged but CCT was not increased and there were no systemic or ocular factors with an effect on CCT. Siribunkum et al.[5] showed in their study on the 60 eyes of 30 diabetic patients that the diabetic corneas tended to be thicker and had more pleomorphism and polymegathism, but this was not statistically significant while the duration of diabetes mellitus correlated significantly with these corneal changes.

Table 3. Multivariate regression analysis results for central corneal thickness

Variables	B	t	p
Constant	544.591	24.595	0.0001
Duration of DM (year)	0.152	0.098	0.922
HbA1c (%)	2.260)	0.979	0.332
FBG (mg/dl)	0.062	0.809	0.422

B: Nonstandardized regression coefficient, t: T value, DM: Diabetes Mellitus, HbA1c: Hemoglobin A1c, FBG: Fasting blood glucose

In contrast, a population-based study by Su et al.[11] showed that a diabetic person had on average 6.5 µm thicker central corneal thickness than a person without diabetes mellitus. CCT was also positively correlated with increasing non-fasting blood glucose level and HbA1c. Lee et al.[10] found that diabetics of over 10 years' duration had thicker corneas, lower corneal endothelium density, lower hexagonality ratios, and higher variation in cell size when compared to diabetics under 10 years' duration. In contrast to this result, independing from the disease duration, Ozcura et al.[20] suggested that CCT was significantly greater in patients with type-2 DM than healthy subjects. Busted et al.[12] studied juvenile diabetic patients with a mean age of 34 years. They found corneal thickness in diabetics to be significantly thicker than healthy subjects, and suggested that this may be one of the earliest detectable changes in diabetic eyes.

A study by Akinci et al.[13] with a similar age to our study showed thicker CCT values in diabetic patients than the control group. HbA1c was the only disease-related parameter in their study. They had a smaller control group (38 healthy subjects) than ours and the mean ages of the groups were not similar, which may have influenced the results. Urban et al.[14] studied diabetic patients with a mean age of 15.3 years and found the mean CCT to be significantly higher in the diabetic group than the control group. They also found that none of the systemic factors was correlated with the CCT.

Some explanations are offered in the literature for the change in CCT values in diabetic eyes. Na/K-ATPase plays an essential role in regulating corneal endothelial hydration and decreased activation of this enzyme has a major effect on corneal hydration control.[21] Some studies[3,12,22] report that diabetes causes dysfunction of the corneal endothelial pump due to a decrease in Na-K ATPase activity and this may result in morphological and permeability-related changes in the corneas. Corneal endothelial dysfunction and increased corneal hydration may cause higher CCT values.[3,10-12,22] Lee et al.[10] reported that younger diabetic corneas have more corneal endothelial pump capacity than older diabetic corneas. This may explain the lack of a difference in CCT values between the young diabetic group and the young control group in our study.

We found that there was no significant difference in CCT values between diabetic pediatric patients and the healthy control group. Taking other studies into account, we feel that the increased CCT in older diabetics[10,11] and the lack of a correlation between CCT and other disease-related parameters[5,9,14] indicate that the CCT changes may be related to age-related corneal structure changes in diabetic patients rather than any effect of diabetes on the cornea.

In conclusion, we found that diabetes mellitus does not affect the corneal thickness in adolescents. We also did not find any disease-related variable that correlated with the CCT. Supporting any result with examination of the endothelial cell structure will make any future study even more valuable.

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