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Central corneal thickness in type II diabetes mellitus: is it related to the severity of diabetic retinopathy?

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Central corneal thickness in type II diabetes mellitus: is it related to the severity of diabetic retinopathy?

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Background/aim: To compare the central corneal thickness (CCT) of type II diabetes mellitus patients with age- and sex-matched healthy subjects and to determine the association of the severity of diabetic retinopathy and CCT.

Materials and methods: Type II diabetes mellitus patients without retinopathy, with nonproliferative retinopathy, and with proliferative retinopathy were organized as the three subgroups of the study group, and an age- and sex-matched control group was formed. All subjects underwent full ophthalmological examination and CCT measurement with ultrasonographic pachymetry. CCT values were compared between diabetic and healthy subjects and between the three diabetic subgroups. Correlation analysis was performed to determine any relationship between CCT and intraocular pressure.

Results: The average CCT was significantly higher in diabetic patients than in the control group ($P = 0.04$). CCT in diabetic patients without retinopathy did not significantly differ from that of patients with retinopathy ($P = 0.64$). Similarly, there was no significant difference in CCT between nonproliferative and proliferative diabetic retinopathy patients ($P = 0.47$). In the whole study population, CCT was significantly correlated with intraocular pressure ($P < 0.01$).

Conclusion: CCT is significantly increased in type II diabetes mellitus patients with respect to controls. Retinal disease severity does not seem to have an effect on corneal thickness.

Key words: Central corneal thickness, diabetes mellitus, diabetic retinopathy, pachymetry

1. Introduction

With well-documented ocular complications, diabetes mellitus (DM) is a leading cause of blindness throughout the world. Although investigations in DM are mostly focused on retinal damage, corneal alterations associated with DM have also been reported (1–4). Prolonged abnormal glucose metabolism results in alterations in the epithelium, stroma, and endothelium of the cornea (5). Central corneal thickness (CCT), which reflects the metabolic status of the cornea, is also influenced by DM (6). These diabetic changes in the cornea might have an influence on intraocular pressure (IOP) measurements. Therefore, in diabetic patients, accurate detection of IOP could be problematic and challenging (7).

In the current study, we aimed to analyze CCT in type II DM patients and to compare the results with age- and sex-matched healthy controls. We also investigated the association of retinal disease severity and CCT among diabetic patients.

2. Materials and methods

The study was done at the Başkent University Adana Research and Clinic Center Department of Ophthalmology. Patients with type II (noninsulin-dependent) DM, who were admitted to our outpatient clinic, were screened for eligibility for the study. A patient who had a referring-physician diagnosis of type II DM and who was given antidiabetic medication was defined as diabetic. Subjects with a prior history of ocular surgery, ocular surface disease, glaucoma, or uveitis and patients who had a history of chronic topical medication use were not involved in the study. Likewise, past or present contact lens wearers were excluded.

This prospective clinical study was consistent with the tenets of the Declaration of Helsinki. Local ethics committee approval was obtained. All patients were informed of the risks and benefits of the procedure and a written informed consent form was obtained from all participants.

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Two hundred seventeen eyes of 217 patients were enrolled. One eye from each patient was used for analysis. Patients with DM were assigned into 3 groups: the first group included 59 patients ranging between the ages of 34 and 75 years (mean: 55 ± 9.8 years) with no diabetic retinopathy (DR), the second group included 55 patients ranging between the ages of 38 and 78 years (mean: 57.1 ± 8.3 years) with nonproliferative diabetic retinopathy (NPDR), and the third group included 51 patients ranging between the ages of 41 and 74 years (mean: 56.3 ± 7.2 years) with proliferative diabetic retinopathy (PDR). The control group consisted of 52 age- and sex-matched healthy subjects ranging between the ages of 38 and 75 years (mean: 56.1 ± 7.5 years). The differentiation of NPDR and PDR was made as previously reported by the Early Treatment Diabetic Retinopathy Study Research Group (8).

All patients underwent full ophthalmological examination, including thorough biomicroscopic indirect funduscopy through the mydriatic pupil. Intraocular pressure was measured by Goldmann's applanation tonometer. Data on age and sex were recorded. Fundus fluorescein angiography was performed whenever necessary (9). CCT was measured by ultrasonographic pachymetry (UP-1000 Ultrasonic Pachymeter, Nidek Co., Aichi, Japan) under topical anesthesia. The average of 5 consecutive readings was recorded. All pachymetry measurements were performed by the same technician between 1000 and 1200 hours to eliminate diurnal variation in corneal thickness.

For statistical analysis, SPSS 11.0 for Windows (SPSS Inc., Chicago, IL, USA) was used. By the Kolmogorov-Smirnov test, the distribution function of the sample was analyzed. In the groups, age, severity of DR, and CCT were compared by ANOVA. Different groups were assigned by post hoc Tukey HSD test. Independent t-test was used to assess the differences among measurements in the 4 groups and the Pearson correlation coefficient was used to investigate the correlation between DM and corneal thickness. The level of significance was set at $P < 0.05$.

3. Results

The male/female ratio of groups 1, 2, and 3 and the controls were 23/36, 28/27, 27/24, and 31/21, respectively. There was no statistical significance by means of age or sex between groups ($P = 0.63$ and $P = 0.34$, respectively).

The mean CCT values of each group are given in Table 1. The average CCT was significantly higher in diabetic patients (including all 3 groups) than in the control group ($P = 0.04$). However, CCT in diabetic patients without retinopathy did not significantly differ from those of patients with retinopathy ($P = 0.64$). Similarly, there was no significant difference in CCT between NPDR and PDR patients ($P = 0.47$).

According to the correlation analysis, in the whole cohort, CCT was significantly correlated with IOP ($P < 0.01$). These two parameters were significantly correlated in both diabetic patients and the controls ($r = 0.279$, $P < 0.01$ and $r = 0.517$, $P < 0.01$, respectively). Table 2 demonstrates the IOP values of groups. Mean IOP values

Table 1. Central corneal thickness (μm) values of groups

	N (eyes)	Mean CCT	95% confidence interval	
			Lower bound	Upper bound
Group 1	59	552.5 ± 38.0	542.5	562.4
Group 2	55	560.0 ± 32.3	551.3	568.7
Group 3	51	550.1 ± 38.3	539.3	560.8
Controls	52	542.7 ± 31.6	533.9	551.5

Table 2. Intraocular pressure values (mmHg) of groups.

	N (eyes)	Mean IOP	95% confidence interval	
			Lower bound	Upper bound
Group 1	59	17.1 ± 3.8	16.1	18.1
Group 2	55	16.4 ± 3.3	15.5	17.3
Group 3	51	15.6 ± 4.0	14.5	16.7
Controls	52	15.5 ± 3.4	14.6	16.4

were higher in diabetic patients than in controls; however, the difference was not significant ($P = 0.061$)

4. Discussion

DM affects the corneal endothelium by altering sodium-potassium ATPase activity; thus, functional changes occur in diabetic corneas (4,10,11). Corneal thickening in both type I and II DM was reported in several studies (2,4,12–15). This increase in corneal thickness reflects the altered functional status of the corneal endothelium and may lead to falsely high IOP measurements.

In this current study, we established age- and sex-matched groups. According to our results, we found thicker corneas in type II diabetic patients. Similarly, Su et al. found that hyperglycemia was associated with increased CCT in their study and explained this finding with mechanisms such as corneal endothelial dysfunction, stromal hydration, and swelling of the cornea (15). Lee et al. reported higher CCT in insulin-dependent DM patients compared to controls (4). Roszkowska et al. compared diabetic subjects who had background diabetic retinopathy with healthy controls and found thicker CCT in the diabetic group (2). Ozdamar et al. also found thicker central corneas among diabetics with respect to nondiabetic controls (14). Recently, Storr-Paulsen et al. studied 107 patients with type II DM and 128 nondiabetic controls and concluded that CCT was increased among type II diabetes patients compared to controls (13).

In a similar study among type I DM patients, Keoleian et al. found that corneal thickness of type I diabetes patients did not significantly differ from the age-matched nondiabetic control subjects. However, they found altered morphology of the endothelium among diabetics (16). Likewise, Inoue et al. and Wiemer et al. did not report any differences in CCT between diabetics and controls (17,18).

In the current study, no significant difference was found in CCT between the three diabetic subgroups. Busted et al. and Wiemer et al. also found that CCT increased in DM regardless of the severity of the retinal disease (12,18). Ozdamar et al. reported in their study that patients with

proliferative retinopathy had thicker CCT than those with nonproliferative retinopathy and no retinopathy; however, the difference was not statistically significant (14).

Other than corneal hydration and swelling, the increase in CCT may also be a result of increased collagen crosslinking due to the accumulation of advanced glycosylation end products, a process related both to diabetes and normal aging. Collagen crosslinking may lead to corneal thickening and gradual stiffening of the cornea and consequently affect the accuracy of IOP measurements (19). The influence of CCT and corneal biomechanics on IOP measurement was shown in a study by Broman et al. (20).

In the current study, CCT was found to be significantly correlated with IOP, as expected. Average IOP values of the diabetic subjects were also higher than those of the healthy controls; however, this difference was not statistically significant. Results of studies with large series have shown that DM is associated with high IOP measurements (21,22). Both increased CCT and increased corneal stiffness due to collagen crosslinking cause overestimation of the IOP in diabetic patients; therefore, diabetes may have a preventive effect on glaucoma progression (5,7). Nevertheless, we think that diabetic patients must be closely followed for IOP rise or glaucoma progression, because, in daily practice, IOP readings might sometimes be overlooked, as the physician usually focuses on retinopathy.

In conclusion, we found increased CCT in type II DM regardless of the severity of the retinal disease. This increase in CCT was correlated with IOP. In our opinion, increased corneal thickness should be kept in mind when measuring and evaluating IOP in diabetic patients. It should be investigated in further studies whether corneal thickness could be an indicator of the metabolic status of DM.

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