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Full Length Research Paper

Corneal biomechanical characteristics, intraocular pressure and central corneal thickness in patients with type 2 diabetes mellitus

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To evaluate corneal biomechanical properties, intraocular pressure and central corneal thickness in type 2 diabetic patients by Ocular Response Analyzer (ORA), ORA measurements were performed on the 80 eyes of 40 diabetic patients (group I) and 80 eyes of 40 healthy people who served as the control group (group II). Corneal hysteresis (CH), corneal resistance factor (CRF), intraocular pressure (Goldmann correlated [IOPg], corneal compensated [IOPcc]) and central corneal thickness (CCT) values were determined by ORA. Mean age of patients with diabetic melitus (DM) and control groups were 51.8 ± 5.8 and 51.2 ± 7.1 years, respectively. Mean CH and CRF were 9.44 ± 0.62 versus 9.41 ± 0.50 (p=0.738) and 11.58 ± 0.60 versus 10.56 ± 0.50 (p<0.001), in groups I and II, respectively. Mean IOPg and IOPcc were 19.90 ± 3.35 mmHg versus 18.90 ± 2.56 mmHg (p=0.036) and 17.41 ± 2.57 mmHg versus 17.22 ± 2.66 mmHg (p=0.651) in groups I and II, respectively. Mean CCT's were 548.02 ± 23.16 versus 521.92±31.60 (p<0.001) in groups I and II, respectively. Statistical analysis revealed significant differences for CRF, IOPg and CCT values between groups. CRF, IOPg and CCT values were altered in diabetics and these changes can be detected by ORA. Further studies are required to establish the effects of type 2 diabetes on corneal biomechanical properties.

Key words: Type 2 diabetes mellitus, ocular response analyzer, corneal biomechanical characteristics, central corneal thickness

INTRODUCTION

Ocular response analyzer (ORA, Reichert; USA) is a non-contact tonometer being developed to measure bio-mechanical features of cornea through monitoring and analyzing corneal response during air impulse (Kotecha, 2007). Two applanation values (P1, P2) are obtained by electro-optic system; one while the cornea undergoes deformation after a rapid air impulse applied to a 3 mm central corneal area and the other as the cornea begins to return to previous form. The difference between these two pressure values is called 'corneal hysteresis' (CH). CH is a valuable indicator of the biomechanical properties (particularly viscous properties) of the cornea. The average of two applanation pressures is determined as Goldmann-correlated IOP (IOPg). The instrument also determines a second IOP value (IOPcc) considering CH, which is compensated with the biomechanical properties of the cornea. Another important parameter of the instrument is the corneal resistance factor (CRF). It is strongly associated with central corneal thickness particularly and

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Table 1. Mean CH, CRF, IOPg, IOPcc, CCT values of the groups.

	CH (mean ± SD) (range)	CRF (mean ± SD) (range)	IOPg (mean ± SD) (range)	IOPcc (mean ± SD) (range)	CCT (mean ±SD) (range)
Group 1	9.44 ± 0.62 (8.30 to 10.90)	11.58 ± 0.60 (10.10 to 12.90)	19.90 ± 3.35 (12.0 to 26.6)	17.41 ± 2.57 (11.0 to 23.4)	548.02 ± 23.16 (500 to 601)
Group 2	9.41 ± 0.50 (7.90 to 10.40)	10.56 ± 0.50 (9.70 to 12.40)	18.90 ± 2.56 (12.70 to 24.50)	17.22 ± 2.66 (11.20 to 21.10)	521.92 ± 31.60 (470 to 591)
p value	0.738	<0.001	0.036	0.651	<0.001

CH, Corneal hysteresis; **CRF,** corneal resistance factor; **IOPg,** Goldmann correlated intraocular pressure; **IOPcc,** corneal compensated intraocular pressure; **CCT**, central corneal thickness; **SD**, standart deviation.

is a good indicator of elastic properties of the cornea (Shah et al., 2006; Saricaoğlu, 2010).

Diabetes is a common disease with high risks of morbidity and early mortality, which leads to acute metabolic complications as well as vascular, renal, retinal or neuropathic disorders in the long-term. The incidence of the Type 2 diabetes (insulin-independent diabetes) that represents 80% of all diabetes cases is estimated to be 2% to 5% in the population. The incidence and prevalence of the Type 2 diabetes is gradually increasing especially in the industrialized countries in which the life style has become largely changed (Halifeoglu et al., 2005).

Diabetes leads to complications in almost all ocular structures, including eyelids, conjunctiva, cornea, extra ocular muscles, iris, lens, and retina. The most important complication leading to the visual loss is diabetic retinopathy. Diabetes may also cause several corneal disorders. A decrease in epithelial adhesion and corneal sensitivity, increased fragility, recurrent epithelial erosions, epithelial edema, decreased corneal sensitivity, neurotrophic ulcers are among the corneal complications in diabetic patients (Totan et al., 2000; Weston et al., 1995; Su et al., 2008). These changes may affect the measurement of IOP in an unexpected manner, such as an overestimation of the “true” IOP. Although the current gold standard to measure IOP is Goldmann applanation tonometry (GAT), it has been clearly documented that GAT measurements can be affected by several ocular factors such as corneal curvature, axial length, and central corneal thickness (CCT). So it is clear that accurate IOP measurements can be determined independently by ORA.

The aim of our study was to investigate whether corneal biomechanical properties, CCT and intraocular pressures of the patients with type 2 diabetes differ from that of control group.

MATERIALS AND METHODS

The study included 40 type 2 diabetic patients and 40 healthy individuals who served as control. All diabetic patients were recruited from the Department of Endocrinology, and all healthy patients were recruited from the General Ophthalmology Clinic.

Exclusion criteria include patients with at least one of the following conditions; topical or systemic treatment for a systemic disorder other than diabetic miletus (DM), previous ocular surgery, previous laser or anti-VEGF (Vascular endothelial growth factor) therapy, ophthalmic trauma history, corneal and lens pathologies preventing ocular fundus examination, uveitis and other posterior segment pathologies. The patients who had proliferative stage diabetic retinopathy were not included in the study because of potential anterior segment complications (for example, iris neovascularization, neovascular glaucoma). All patients gave informed consent to be enrolled in the study. All procedures were performed in accordance with the Declaration of Helsinki.

CH, CRF measurements, IOPg, IOPcc and CCT values were measured by ORA after ophthalmologic examination including visual acuity with and without correction, anterior segment examination, and fundus examination after pupil dilation of the patients. Measurements were performed by the same operator and the average of 5 values obtained from one measurement for each eye was used for analysis.

For statistical assessment, SPSS 11.0 was used. Results are reported as mean ± SD. P value less than 0.05 was considered as statistically significant. Differences between groups were analyzed by Independent T test (parametric). To assess the correlation of the data with normal distribution, Kolmogorov-Smirnov test was used.

RESULTS

The mean age of the patients in the group 1 was 51.8 ± 5.8 years (range, 39 to 66) and 51.2 ± 7.1 (range, 39 to 66) in group 2. No significant difference was found between the groups regarding age and gender ($p = 0.56$).

Table 1 shows the results of mean CH, CRF, IOPg, IOPcc and CCT values of the patients in the group 1 and group 2.

CRF ($p<0.001$), IOPg ($p=0.036$) and CCT ($p<0.001$) values were statistically different between groups. There were no statistically significant differences regarding CH ($p=0.738$) and IOPcc ($p=0.651$) (Figures 1 and 2).

The correlation analyses for CH and CRF in the diabetic patients and the control groups are shown in Tables 2 and 3, respectively. CH and CRF showed a correlation with CCT and IOPg.

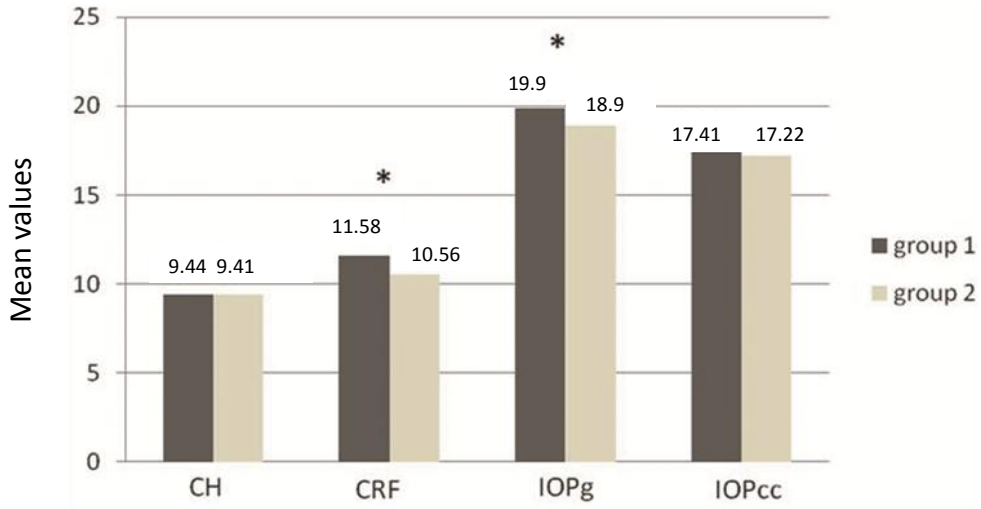

Figure 1. Comparison of the mean CH, CRF, IOPg, IOPcc values. **CH,** Corneal hysteresis; **CRF,** corneal resistance factor; **IOPg,** Goldmann correlated intraocular pressure; **IOPcc,** corneal compensated intraocular pressure; *, statistical significance.

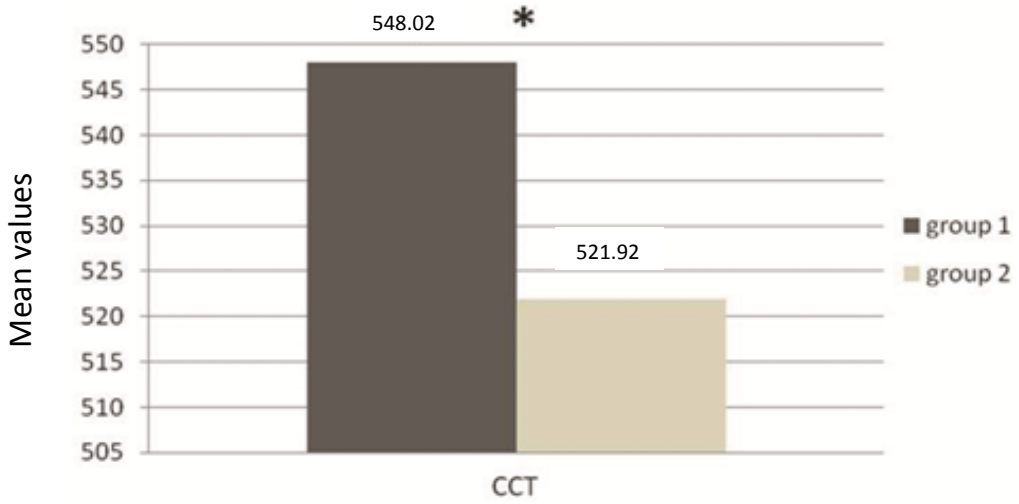

Figure 2. Comparison of the mean CCT values of the groups . **CCT,** central corneal thickness; *, statistical significance.

Table 2. Results of correlation analyses for CH and CRF in healthy control subjects.

Parameters	Age	CCT	IOPg
CRF			
r	0.20	0.72	0.73
p	**0.04**	**0.0001**	**0.0001**
CH			
r	0.18	0.56	0.61
p	0.13	**0.0001**	**0.0001**

Bold type shows statistical significance.

Table 3. Results of correlation analyses for CH and CRF in diabetic patients.

Parameters	Age	CCT	IOPg
CRF			
r	-0.11	0.78	0.61
p	0.27	**0.0001**	**0.0001**
CH			
r	-0,12	-0.24	-0.28
p	0.31	**0.01**	**0.01**

Bold type shows statistical significance.

DISCUSSION

The potential pathologies that may occur in the cornea of diabetic patients are epithelial edema, Descemet membrane folds, recurrent erosions, neurotrophic ulcers, delayed wound healing and decrease in corneal sensitivity (Keoleian et al., 1992). In some studies conducted with specular microscopy, it was shown that certain morphologic changes occurred in the cornea endothelium compared with the healthy individuals and it was argued that these changes might be due to chronic metabolic stress resulting from hyperglycemia (Schultz et al., 1984; McNamara et al., 1998).

McNamara et al. (1998) reported that in diabetic patients, hyperglycemia alters the corneal structure by impairing the hydration of the cornea. Sanchez-Thorin (1998), reported that diabetes impairs homeostasis in the corneal epithelium, epithelial basal membrane and basal membrane complex, corneal tissues such as stroma and endothelium, and consequently leads to structural changes in these tissues. In the light of that information, in our study, the structural changes that occurred in the cornea of diabetic patients were evaluated with ORA device that displays corneal biomechanical properties, one of the important issues, which the studies have recently focused on.

Although the Goldmann applanation tonometry is the most widely used method today in the clinical practice to measure intraocular pressure, it has been shown that this method is affected by many ocular parameters (for example, corneal thickness, refractive errors, corneal edema and corneal surface irregularities) (Saricaoğlu, 2010). Clinical studies conducted with ORA have shown that this device is not affected or slightly affected by central corneal thickness (CCT) (Kotecha, 2007; Saricaoğlu, 2010). There were no differences between groups regarding IOPcc in our study despite statistically higher IOPg in group 1 which is in favor of this situation. Studies show that eyes in patients with diabetes have a greater central corneal thickness (CCT) and that there is a positive association between CCT and the degree of diabetic retinopathy. During the past decade, it has been proposed that CCT is one of several corneal biomechanical properties that affect IOP measurement. Those biomechanical properties include corneal viscosity, elasticity, hydration, connective tissue composition, and regional pachymetry (Chang and Stulting, 2005). In a recent study, it was shown that the level of corneal elasticity may influence the effect of CCT on IOP measurement. Recently, it has been shown that tonometry is affected by all corneal biomechanical characteristics other than CCT (Liu and Roberts, 2005).

Diabetic eyes with the same CCT varied greatly in CH and CRF when compared to normal eyes. Several investigators have reported that CH and CRF are correlated with CCT, as we saw in our study. The cornea responds to a pressure first with deformation and then with relaxation. However, deformation and relaxation pathways differ from each other; energy loss described by these different responses defines corneal hysteresis (CH) represents the ability of the cornea to stretch against a force and then to revert to the previous status. CH is a good indicator of the biomechanical properties of the cornea (Kotecha et al., 2010). It is defined by the difference between two applanation pressures (Saricaoglu, 2010). In a study by Kotecha et al. (2010), it was shown that CH value of diabetic patients did not statistically and significantly differ in comparison with the control group. In other studies, (Goldich et al., 2009; Hager et al., 2009) denoted that CH value of diabetic patients did not statistically and significantly differ in comparison with normal control group, however, CH value of the patients with type 1 diabetes was significantly higher than that of type 2 diabetics. In contrast, in a study performed by Sahin et al. (2009), it was reported that CH value of diabetic patients was significantly lower compared to the control group. In our study, we did not find any statistically significant differences between two groups regarding CH values.

Another important parameter measured by ORA is corneal resistance factor (CRF). It is partly independent from IOP. It is highly correlated with particularly CCT.

This parameter reflects the elastic properties of the cornea better; whilst, CH is a good indicator of the viscous properties of the cornea (Krueger and Ramos-Esteban, 2007). In our study, CRF was statistically and significantly higher in the diabetic patients. In a study by Kotecha et al. (2010), this value was higher in diabetic patients. Similarly, Goldich et al. (2009) showed that CRF value of diabetic patients were higher than that of the control group. Also, several other studies reported higher central corneal thickness (CCT) in diabetic patients which is parallel to that increase in CRF value (Weston et al., 1995; Su et al., 2008). In our study, parallel to these results, we found that CCT values of diabetic patients were significantly higher compared to the control group.

Co-existence of diabetes and glaucoma has been reported in many studies. In diabetic patients, higher IOP values were found than the normal population (Bonovas et al., 2004). The Goldmann applanation tonometry sets the corneal thickness to be 520 µ. It misleads to high IOP measurements in thick corneas and low IOP measurements in thin corneas (Chihara, 2008). Pathologies causing alterations in the viscoelastic structure of the cornea may impede a correct IOP measurement. It is debated that these routine tonometry methods that we used may cause false IOP measurements when the rigidity of the cornea is affected (high IOP, keratoconus, corneal dystrophies, previous photorefractive surgeries). To minimize these errors, 2 distinct IOP values may be measured with ORA device. IOPg is an average of two applanation pressures; IOPcc is a second IOP value compensated with the biomechanical properties of the cornea considering CH value. That IOPg of the group 1 was statistically and significantly higher than that of the group 2 in our study and is parallel to the studies in the literature reporting that IOP increases in diabetic patients, however, that there was no statistical difference between two groups for IOPcc values suggests that certain alterations in the parameters affecting corneal thickness occur in diabetic patients.

In conclusion, ORA device is able to detect the changes that may occur in corneal parameters of the patients with type 2 diabetes. Clinicians should take this finding into account in routine practice because clinically relevant IOP measurements errors may independent of CCT occur. To evaluate the effects of these changes occurring in the cornea on the corneal refractive power and IOP, further studies are needed.

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