Journal of Diabetes and Its Complications xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

Corneal thickness differences between type 2 diabetes and non-diabetes subjects during preoperative laser surgery examination

Juan A. Sanchis-Gimeno [a,*], Luis Alonso [b], Mohammed Rahhal [b], Markus Bastir [c], Marcelino Perez-Bermejo [a], Lurdes Belda-Salmeron [a]

[a] Ocular Anatomy Unit, Department of Anatomy and Human Embryology, Faculty of Medicine, University of Valencia, Avda. Blasco Ibanez 15, E46010, Valencia, Spain
[b] Rahhal Ophthalmology Clinic, Calle de Cirilo Amoros, 52, E46004, Valencia, Spain
[c] National Museum of Natural Sciences – CSIC, Calle de Jose Gutierrez Abascal, 2, E28006, Madrid, Spain

ARTICLE INFO

Article history:
Received 9 June 2016
Received in revised form 2 August 2016
Accepted 22 August 2016
Available online xxxx

Keywords:
Corneal thickness
Laser refractive surgery
Quantitative anatomy
Scanning-slit corneal topography
Type 2 diabetes

ABSTRACT

Aims: To evaluate the differences in corneal thickness between type 2 diabetes subjects with HbA1c under 7.0% and non-diabetes subjects during their preoperative laser surgery examinations.
Methods: The mean of five consecutive corneal thickness measurements at the central and mid-peripheral cornea was obtained by means of noncontact scanning-slit corneal topography (Orbscan Topography System II; Orbscan, Inc., Salt Lake City, UT, USA) in 35 myopic non-insulin dependent type 2 diabetes subjects (17 males and 18 females) and 48 healthy myopic controls (23 males and 25 females).
Results: The corneal thickness values at the central and mid-peripheral cornea were significantly higher in the diabetic group ($p < .001$). The diabetic subjects presented the highest thickness value in the superior cornea ($n = 22$; 62.9%) followed by the nasal ($n = 9$; 25.7%) and the temporal ($n = 4$; 11.4%) cornea, but never in the inferior cornea. The control subjects presented the highest thickness value in the superior cornea ($n = 19$; 39.6%) followed by the nasal ($n = 18$; 37.5%), the inferior ($n = 6$; 12.5%), and the temporal ($n = 3$; 6.3%) cornea. The central corneal thickness (CCT) of the diabetes patients was not statistically correlated with their HbA1c ($r^2 = .078$; $p = .104$), body mass index ($r^2 = .007$; $p = .633$), and time from diagnosis of diabetes ($r^2 = .025$; $p = .363$), but it was correlated with their corneal endothelial cell density values ($r^2 = .543$; $p < .001$).
Conclusions: Diabetes subjects with HbA1c under 7.0% who are candidates for laser refractive surgery present thicker corneas than their age-matched control subjects. In these patients, there is a correlation between their CCT values and their corneal endothelial cell density values, so when higher CCT values were found, lower corneal endothelial cell density values were observed.

1. Introduction

In recent years, several papers have evaluated the changes in central corneal thickness (CCT) associated with diabetes mellitus with conflicting results. Some studies report higher CCT values in diabetic patients compared with non-diabetic control subjects (Busted, Olsen, & Schmitz, 1981; Calvo-Maroto, Cerviño, Perez-Cambrodí, García-Lázaro, & Sanchis-Gimeno, 2015; Lee, Oum, Choi, Lee, & Cho, 2006; Ozdamar et al., 2010; Roszkowska, Tringali, Colosi, Squeri, & Ferreri, 1999; Storr-Paulsen, Singh, Jeppesen, Norregaard, & Thulesen, 2014; Su, Wong, Wong, et al., 2008), while others found no statistically significant differences in CCT between diabetic and control groups (Choo et al., 2010; Inoue, Kato, Inoue, Amano, & Oshika, 2002; Keoleian, Pach, Hodge, Trocme, & Bourne, 1992; Larsson, Bourne, Pach, & Brubaker, 1996; Sánchez-Thorin, 1998; Schultz, Matsuda, Yee, Edelhauser, & Schultz, 1984; Schultz, Van Horn, Peters, Klewin, & Schutten, 1981; Siribunkum, Kosrirukvongs, & Singalavanija, 2001).

In addition, laser refractive surgery is one of the most common surgeries performed with almost one million people undergoing corneal refractive surgery every year in the United States alone (Bower & Woreta, 2014). While it is known that uncontrolled diabetic disease is an absolute contraindication for laser refractive surgery (Spadea & Paroli, 2012), some authors have observed that patients with well-controlled diabetes present good refractive outcomes (Halkiadakis, Belfair, & Gimbel, 2005).

Following on from this, the aim of the present study was to evaluate the corneal thickness of myopic type 2 diabetes patients with HbA1c under 7.0% who required excimer laser surgery and to ascertain whether these patients present corneal thickness differences when compared with an age-matched myopic control group.

2. Methods

2.1. Patients

A prospective study involving 35 patients (17 males and 18 females) with non-insulin dependent type 2 diabetes and 48 healthy control

Conflict of interest: The authors declare that they have no conflict of interest.

* Corresponding author at: University of Valencia, Faculty of Medicine, Department of Anatomy and Human Embryology, Av. Blasco Ibanez, 15, Valencia, E-46010, Spain.
E-mail address: juan.sanchis@uv.es (J.A. Sanchis-Gimeno).

http://dx.doi.org/10.1016/j.jdiacomp.2016.08.024
1056-8727/

subjects (23 males and 25 females) with a manifest spherical equivalent refraction ranging from −1 to −4.50 diopters (Lleó-Pérez & Sanchis-Gimeno, 2007) was performed in order to ascertain the differences in the corneal thickness between diabetes patients and age-matched healthy subjects. All the patients were diagnosed with type 2 diabetes in accordance with the guidelines of the American Diabetes Association (American Diabetes Association, 2010): 1. A1C ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay; or 2. FPG ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h; or 3. 2-h plasma glucose ≥200 mg/dl (11.1 mmol/l) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water; or 4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dl (11.1 mmol/l). In the absence of unequivocal hyperglycemia, criteria 1–3 should be confirmed by repeat testing.

Both groups of subjects (diabetes and non-diabetes subjects) wanted to undergo laser refractive surgery and had a complete ophthalmologic examination that included refraction, slit-lamp evaluation, pachymetry, corneal esthesiometry, Goldmann applanation tonometry, and binocular indirect ophthalmoscopy fundus examination through dilated pupils (Ahuja, Baratz, McLaren, Bourne, & Patel, 2012; Calvo-Maroto et al., 2015).

Inclusion criteria comprised patients diagnosed with type 2 diabetes in accordance with the guidelines of the American Diabetes Association (American Diabetes Association, 2010) with HbA1c under 7.0% (twice during the previous six months, the last HbA1c measurement carried out one week before the corneal thickness measurements), and with myopia that ranged from −1.00 to −4.50 diopters (Lleó-Pérez & Sanchis-Gimeno, 2007). Control subjects comprised healthy subjects with myopia that ranged from −1.00 to −4.50 diopters (Lleó-Pérez & Sanchis-Gimeno, 2007).

Exclusion criteria comprised previous corneal or intraocular surgery, history of corneal and/or ocular disease (i.e. keratectasia, cataract, decreased corneal sensation, diabetic retinopathy, etc.), intraocular inflammation, contact lens wear, and Goldmann applanation tonometry ≥21 mm Hg. Patients with systemic diseases, other than diabetes mellitus, and subjects taking any kind of medication, except drugs for diabetes control, were also excluded (Ahuja et al., 2012; Calvo-Maroto et al., 2015).

From an initial sample of 268 volunteers, 107 (39.2%) diabetes subjects and 78 (29.1%) non-diabetes subjects were excluded from the study after application of the inclusion and exclusion criteria. The reasons for exclusion of 107 (100%) diabetes subjects were the presence of HbA1c >7.0% ($n = 39$; 36.4%), systemic diseases like hypercholesterolemia and hypertension ($n = 21$; 19.6%), contact lens wear ($n = 17$; 15.9%), spherical equivalent refraction >4.50 diopters ($n = 14$; 13.1%), diabetic retinopathy ($n = 9$; 8.4%), tonometry ≥21 mm Hg ($n = 5$; 4.7%), previous retinal detachment ($n = 1$; 0.9%), and keratectasia ($n = 1$; 0.9%). The reasons for exclusion of 78 (100%) non-diabetes subjects were the presence of contact lens wear ($n = 31$; 39.7%), spherical equivalent refraction >4.50 diopters ($n = 26$; 33.3%), systemic diseases like hypercholesterolemia and hypertension ($n = 10$; 12.8%), tonometry ≥21 mm Hg ($n = 9$; 11.5%), and previous corneal surgery ($n = 2$; 2.6%).

2.2. Corneal thickness measurements

Corneal thickness was recorded by an experienced physician, who was unaware of the subjects' clinical background, using a noncontact scanning-slit corneal topography system (Orbscan Topography System II; Orbscan, Inc., Salt Lake City, UT, USA). The mean of five consecutive measurements was obtained from each eye at the central cornea and at superior, inferior, nasal, and temporal locations with a distance of 3 mm from the visual axis (Sanchis-Gimeno, Lleo-Perez, Alonso, Rahhal, & Martínez-Soriano, 2004).

All corneal thickness measurements were carried out from 10.00 a.m. to 11.00 a.m. to avoid diurnal variations and at least three hours after the patients' awakening (Harper, Boulton, Bennett, et al., 1996; Lattimore, Kaupp, Schallhorn, & Lewis, 1999). During examination, the temperature ranged from 18° to 22 °C and the relative humidity ranged from 38% to 45%.

2.3. Statistics

In the present study, only one eye of each subject was used for statistical analysis. G*Power 3 (version 3.0.10) was used to calculate the statistical power of the current study (Faul, Erdfelder, Lang, & Buchner, 2007). We studied a total sample size of $n = 83$ with 35 and 48 subjects included in the diabetic and control groups, respectively, and a value of α error probability = 0.05 (corresponding to α level of 5%); the statistical power reached was 0.83. Normality of the data distribution was determined using the Shapiro–Wilk test. Student's t-test was used to assess differences between groups. Regression analysis with coefficient of determination was used to assess a possible relationship between CCT and the HbA1c levels, body mass index (BMI), time from diagnosis of diabetes and corneal endothelial cell density values. P value <.05 was considered statistically significant. All statistical analyses were performed using SigmaPlot v12 software (Systat Software, Inc., San Jose, CA, USA). Data are reported as mean ± standard deviation (SD).

3. Results

The demographic data of the diabetic and control groups are summarized in Table 1. The corneal thickness values at the central and mid-peripheral cornea were significantly higher for the diabetic group (Table 2). The CCT of the diabetes patients was not statistically correlated with HbA1c ($r^2 = .078$; $p = .104$), BMI ($r^2 = .007$; $p = .633$), or time from diagnosis of diabetes ($r^2 = .025$; $p = .363$). Nevertheless, the CCT of the diabetes patients was statistically correlated with their corneal endothelial cell density ($r^2 = .543$; $p < .001$), so when higher CCT values were found, lower corneal endothelial cell density values were observed.

The minimum thickness value was always found in the central cornea in both diabetic and control subjects. The diabetic subjects presented the highest thickness most commonly in the superior cornea ($n = 22$; 62.9%) followed by the nasal ($n = 9$; 25.7%) and the temporal ($n = 4$; 11.4%) cornea, but never in the inferior cornea. The control subjects presented the highest thickness most commonly in the superior cornea ($n = 19$; 39.6%) followed by the nasal ($n = 18$; 37.5%), the inferior ($n = 6$; 12.5%), and the temporal ($n = 3$; 6.3%) cornea.

The mean difference between the CCT and the maximum thickness obtained in the peripheral cornea was 104.6 ± 18.1 μm (range 64 to 144 μm) and 120.7 ± 23.8 μm (range 51 to 168 μm) for the diabetic and control groups, respectively ($p < .001$; Student's t-test). The mean difference between the CCT and the minimum peripheral corneal thickness was 67.2 ± 18.6 μm (range 42 to 94 μm) and 58.9 ± 17.9 μm (range 26 to 100 μm) for the diabetic and control groups, respectively ($p < .001$; Student's t-test).

4. Discussion

Patients with diabetes mellitus often present systemic complications, including ocular disorders. Diabetic retinopathy is the most frequent ocular complication (Stanga, Boyd, & Hamilton, 1999; Williams et al., 2004). Clinical evidence shows that patients with diabetes may develop complications, such as recurrent corneal erosions, superficial punctate keratitis, persistent epithelial defects, impaired wound healing, and decreased corneal sensitivity (Sánchez-Thorin, 1998; Schultz et al., 1981, 1984; Siribunkum et al., 2001). Currently, however, diabetic patients are candidates for laser refractive surgery if their diabetes is well controlled (Simpson, Moshirfar, Edmonds, & Christiansen, 2012). Thus, awareness

Please cite this article as: Sanchis-Gimeno, J.A., et al., Corneal thickness differences between type 2 diabetes and non-diabetes subjects during preoperative laser surgery examination, *Journal of Diabetes and Its Complications* (2016), http://dx.doi.org/10.1016/j.jdia-