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The change in central corneal thickness after successful control of hyperglycemia in diabetic patients

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糖尿病患者成功控制高血糖后中央角膜厚度的变化

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摘要

目的:研究糖尿病患者中央角膜厚度与血糖浓度(糖化血红蛋白,HbA1c)的关系。

方法:对 52 例 HbA1c>7% 的 2 型糖尿病患者行单中心、前瞻性临床试验。结果显示,平均随访 6mo 后,血糖浓度控制效果不佳。记录性别、病程,采用超声波测厚仪测量中央角膜厚度,取三次测量的平均值。患者在内分泌科门诊进行治疗。当 HbA1c≤7% 时,再次记录中央角膜厚度,并比较治疗前后的 HbA1c 水平和中央角膜厚度。

结果:治疗前后平均中央角膜厚度分别为 552.30±29.26μm 和 542.36±27.20μm,平均 HbA1c 水平分别为(9.36±1.79)% 和(6.45±0.70)%,差异显著(P=0.0001,配对 t 检验)。

结论:中央角膜厚度随 HbA1c 水平的降低(血糖控制良好)而显著下降,但高血糖和正常血糖患者中央角膜厚度平均值均在正常范围内。因此,在对糖尿病患者进行眼部检查时应注意 HbA1c。

关键词:中央角膜厚度;糖尿病;糖化血红蛋白;眼压;治疗

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Abstract

• AIM: To study the central corneal thickness (CCT) in diabetic patients and its relationship with glycemic control (HbA1c levels).

• METHODS: Single-centre, prospective, clinical trial with a mean of 6-month follow-up examination. We included 52 patients with type 2 diabetes mellitus (DM) whose HbA1c levels were above 7%, indicating poor glycemic control. Sex of patients, and duration of DM were recorded. CCT was determined with ultrasound pachymeter. Each CCT measurement was the mean of 3 pachymeter readings. Then the patients were treated by the endocrinology clinic. When glycemic control was achieved (HbA1c ≤ 7%), CCT measurements were recorded again. HbA1c and CCT before and after treatment were compared.

• RESULTS: Mean CCT before treatment was 552.30 ± 29.26μm, and mean HbA1c was (9.36 ± 1.79)%. Mean CCT after treatment was 542.36 ± 27.20μm, and mean HbA1c was (6.45±0.70)%. The difference between these two values was statistically significant (P=0.0001, paired t test).

• CONCLUSION: Even though mean hyperglycemic and euglycemic CCT measurements were in normal range, CCT decreases significantly by lowering HbA1c level (good glycemic control). Therefore, glycemic status (HbA1c) should be considered when examining the eye of diabetic patients.

• KEYWORDS: central corneal thickness; diabetes mellitus; hemoglobin A1c; intraocular pressure; treatment
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INTRODUCTION

Corneal abnormalities that occur in diabetes mellitus (DM) are termed as diabetic keratopathy. Several clinical studies have shown that patients with diabetes have abnormalities such as higher corneal autofluorescence, lower corneal sensitivity, greater corneal thickness, less endothelial density[1,2].

Corneal endothelium plays a major role in maintaining the optical transparency of the cornea. These cells have limited mitotic capacity and chronic metabolic changes on the cellular level seems to affect the monolayer of corneal endothelial cells[3,4].

Some previous studies showed increased central corneal thickness (CCT) in diabetic patients compared to non-diabetic control groups[1,2], but some others showed no difference in CCT between diabetic and control groups[3,4].

We have not seen any previous study comparing CCT before and after treatment of the same diabetic patients. The purpose of this study was to evaluate CCT in diabetic patients with poor glycemic control and whether there will be a significant change in these measurements after successful control of hyperglycemia.

SUBJECTS AND METHODS

A clinical prospective study, including 52 patients with type II diabetes mellitus whose serum HbA1c levels were above 7%, was performed.

An informed consent was obtained from all patients. The study protocol was approved by the institution's ethics commitee in accordance with the Declaration of Helsinki.

Ophthalmic examination including medical history, biomicroscopic examination of anterior segment, dilated fundus examination with 90D lens were performed. Any patients having history of ocular disease, previous ophthalmic surgery, using topical ocular medications and wearing contact lenses were exluded from study. Age and sex of patients, and duration of DM were recorded.

Corneal thickness was determined with ultrasound pachymeter (PacScan 300AP, Sonomed/Escalon™). Measurements were taken from both eyes during morning hours. Each CCT measurement was the mean of 3 pachymeter readings. Measurements were completed on each eye and these were averaged to provide a single value as described in a previous study done by Lee *et al*[5]. Before doing this, we made a Pearson correlation test to show the correlation between the measurements of both eyes.

Then the patients were treated by the endocrinology clinic. The follow-up of patients was done by different physicians at the endocrinology clinic. After mean follow-up of 6mo (4-8mo) when glycemic control was achieved (HbA1c ≤7%, euglycemic status), CCT measurements were recorded again. HbA1c and CCT before and after treatments were compared. Also association between CCT and sex, duration of DM, and treatment modalities were studied.

Statistical Analysis Statistical analysis were performed by paired *t* test, independent samples *t* test, and *P* values 0.05 or less were considered statistically significant. Values are shown as mean±SD.

RESULTS

There were 52 diabetic patients with poor glycemic control (HbA1c≥7%) in study group. Mean age was 58.75 (46-73) years and there were 27 men (51.9%) and 25 women (48.1%). Duration of diabetes was more than 10 years in 32 patients (61.5%).

Antidiabetic treatment consisted of insulin in 24 patients (46.2%) and oral antidiabetics in 28 patients (53.8%).

At the beginning mean HbA1c level (hyperglycemic condition) was (9.36±1.79)% and after achieving glycemic control (euglycemic condition) mean HbA1c level was (6.45%±0.70)%.

Pearson correlation was 0.88 between the CCT of the right eye and CCT of the left eye. This value showed that CCT measurement of any eye could be used. So we used the single average value. Mean CCT before treatment (hyperglycemic status) was 552.30±29.26μm with range (504-604μm) and after diabetic treatment (euglycemic status) was 542.36±27.20μm with range (495-596μm). The difference was statistically significant (*P*=0.0001, paired *t* test) (Table 1). No statistically significant difference was found in terms of gender, duration of DM and antidiabetic treatment modalities (*P*=0.53; *P*=0.34; *P*=0.54 respectively) (Table 2).

Table 1 Comparison of the patients' mean HbA1c and CCT values before and after successful treatment of type 2 diabetes mellitus $\bar{x}\pm s$

Patients (*n*=52)	Before treatment	After treatment	*P*
HbA1c values (%)	9.36±1.79	6.45±0.70	[1]0.0001
CCT (μm)	552.30±29.26	542.36±27.20	[1]0.0001

CCT: Central corneal thickness. [1]Statistically significant; paired *t* test.

DISCUSSION

Various types of corneal disorders, termed diabetic keratopathy, are common in persons with DM. Reduced tear production, decreased corneal sensitivity, and changes in endothelial morphology and function, alterations of corneal epithelial basement membrane and increased corneal thickness have been documented in diabetic patients[6].

CCT changes associated with DM have been reported in various studies[5-10]. Lee *et al*[5] measured CCT of diabetic patients and found higher CCT values in patients with DM compared with control group. They also found that CCT was thicker in patients with diabetes of over 10 years. These changes may be associated with blood glucose concentrations[11]. We have found a slight increase in CCT of our diabetic patients with more than 10 years' duration when compared to less than 10 years' duration, but it was not statistically significant.

Unlike previous studies which comparing CCT in diabetic patients and in control groups, we assessed the change in CCT measurements in the same diabetic patient group before and after achieving a good glycemic control[2,7,8].

The results of our study showed that mean CCT was thicker in hyperglcemic condition than euglycemic condition in the same patients.

In our study, we did not find a significant difference in CCT in relation to the duration of diabetes, although the mean CCT was thicker in patients with diabetes of over 10 years. Interestingly, mean initial HbA1c level of patients with diabetes of over 10 years was less than the patients with diabetes of shorter duration. This finding may be explained by shorter life span of erythrocytes due to chronic metabolic disease. As a result, young red blood cells which are devoid of glucose accumulation enter into the circulation and lower HbA1c concentration[12].

Choo *et al*[8] found that endothelial cell density in diabetic group was significantly less than that in control group, and CCT was higher in diabetic patients although it was not significant. Also they found that duration of DM and HbA1c levels were not significantly correlated with corneal endothelial findings.

Table 2 Comparison of the patients' mean initial and last HbA1c and CCT values by gender, duration of diabetes, and treatment of diabetes

Patient groups	*n* (%)	Initial HbA1c (%)	Last HbA1c (%)	[1]*P*	Initial CCT (μm)	Last CCT (μm)	[1]*P*
Gender							
M	27 (51.9)	9.77±2.00	6.50±0.74	[3]0.0001	554.74±31.73	542.70±30.35	[3]0.0001
F	25 (48.1)	8.92±1.44	6.39±0.68	[3]0.0001	549.68±26.74	542.00±23.97	[3]0.0001
[2]*P*		0.08	0.57		0.53	0.92	
Diabetes duration							
<10a	20 (38.5)	10.03±2.27	6.67±0.69	[3]0.0001	547.40±26.69	536.45±24.73	[3]0.0001
≥10a	32 (61.5)	8.94±1.28	6.30±0.68	[3]0.0001	555.37±30.77	546.06±28.39	[3]0.0001
[2]*P*		[3]0.03	0.07		0.34	0.21	
Therapy of diabetes							
Insulin	24 (46.2)	10.04±1.91	6.58±0.73	[3]0.0001	549.58±29.12	538.12±27.08	[3]0.0001
Oral anti-diabetic	28 (53.8)	8.77±1.48	6.33±0.67	[3]0.0001	554.64±29.71	546.00±27.27	[3]0.0001
[2]*P*		[3]0.01	0.19		0.54	0.30	

CCT: Central corneal thickness. [1]*P*: Comparison between initial and last measurements was made by paired-*t* test; [2]*P*: Comparison between initial-initial and last-last measurements was made by independent samples *t* test; [3]Statistically significant difference.

Storr-Paulsen *et al*[2] showed a significant increase in CCT in type 2 diabetic group (538 *vs* 546μm) and no correlation with HbA1c level. They also found that in diabetic group, lower endothelial cell count were associated with higher HbA1c values ($P\leqslant0.05$).

Ozdamar *et al*[7] found significantly greater CCT measurements in diabetic eyes compared with control eyes. The mean CCT was greater in eyes with proliferative diabetic retinopathy (PDR) compared with those with non proliferative diabetic retinopathy and no diabetic retinopathy, but difference was not statistically significant. This may be explained as patients devoloping PDR, evidently have bad glycemic control.

Su and co-workers examined the relationship of diabetes and hyperglycemia with CCT and demonstrated mean CCT was 6.5μm thicker in diabetic patients than in persons without diabetes. And this difference was significant ($P\leqslant0.001$)[13].

There are some studies investigating the effects of glycemic control on refraction in diabetic patients. Huntjens *et al*[14], and Li *et al*[15], showed that short term variation in CCT was similar in control subjects and the diabetic patients. There was no significant difference between groups, even though the diabetic corneas were thicker compared to controls. This suggests that short term changes in blood glucose levels do not have a significant effect on CCT in diabetic patients[14,15].

In our study we found a correlation between corneal thickness and the higher HbA1c values. HbA1c reflects the mean blood glucose level during the preceding 6 to 8wk, it reflects the patients' general tendency to diabetes control.

We found that CCT decreased significantly with the change from hyperglycemic status to euglycemic status as reflected by the measurements of HbA1c, in our diabetic patients. We think that this finding will be useful in clinical practice in the evaluation of IOP measurements of diabetic patients.

Patients with type 2 DM have an increased risk of developing open angle glaucoma. Diabetes affects corneal biomechanics, this results in lower corneal hysteresis values than those in healthy control subjects[16,17]. This may cause high intraocular pressure (IOP) measurements. Goldman applanation tonometry (GAT) estimates IOP by measuring the force required to flatten an area of cornea, so corneal characteristics including its thickness can affect IOP measurements. Thicker central corneas may lead to overestimation of the real IOP in diabetic patients[18]. Biswas *et al*[19] confirmed this correlation between increasing IOP and increasing CCT as measured by GAT in diabetic patients.

It was shown that every 10μm change in CCT could yield 0.47-0.98mmHg deviation in IOP measurements by non contact tonometer[20], and 0.28-0.37mmHg deviation by GAT[21].

In conclusion, we found that, even though mean hyperglycemic and euglycemic CCT measurements were in normal range, CCT decreases significantly by lowering HbA1c level (good glycemic control). There is no previous report known to us that evaluated the change in CCT between diabetic patients with poor glycemic control and the same patients after achieving good glycemic control. Glycemic status (HbA1c) should be considered when examining the eye of diabetic patients.

REFERENCES

1 Sánchez-Thorin JC. The cornea in diabetes mellitus. *Int Ophthalmol Clin* 1998;38(2):19-36

2 Storr-Paulsen A, Singh A, Jeppesen H, Norregaard JC, Thulesen J. Corneal endothelial morphology and central thickness in patients with type II diabetes mellitus. *Acta Ophthalmol* 2014;92(2):158-160

3 Hugod M, Storr-Paulsen A, Norregaard JC, Nicolini J, Larsen AB, Thulesen J. Corneal endothelial cell changes associated with cataract surgery in patients with type 2 diabetes mellitus. *Cornea* 2011;30(7):749-753

4 Sudhir RR, Raman R, Sharma T. Changes in corneal endothelial cell density and morphology in patients with type 2 diabetes mellitus: a population-based study, Sankara Nethralaya Diabetic Retinopathy and Molecular Genetics Study (SN-DREAMS, Report 23). *Cornea* 2012;31

(10):1119-1122
5 Lee JS, Oum BS, Choi HY, Lee JE, Cho BM. Differences in corneal thickness and corneal endothelium related to duration in diabetes. *Eye* 2006;20(3):315-318
6 Yin J, Huang J, Chen C, Gao N, Wang F, Yu FS. Corneal complications in streptozosin-induced type 1 diabetic rats. *Invest Ophthalmol Vis Sci* 2011;52(9):6589-6596
7 Ozdamar Y, Cankaya B, Ozalp S, Acaroglu G, Karakaya J, Ozkan SS. Is there a correlation between diabetes mellitus and central corneal thickness? *J Glaucoma* 2010;19(9):613-616
8 Choo M, Prakash K, Samsudin A, Soong T, Ramli N, Kadir A. Corneal changes in type II diabetes mellitus in Malaysia. *Int J Ophthalmol* 2010;3(3):234-236
9 Nishitsuka K, Kawasaki R, Kanno M, Tanabe Y, Saito K, Honma K, Oizumi T, Daimon M, Kato T, Kayama T, Yamashita H; Funagata Study. Determinants and risk factors for central corneal thickness in Japanese persons: the Funagata Study. *Ophthalmic Epidemiol* 2011;18(5):244-249
10 Akinci A, Bulus D, Aycan Z, Oner O. Central corneal thickness in children with diabetes. *J Refract Surg* 2009;25(11):1041-1044
11 Kotecha A, Oddone F, Sinapis C, Elsheikh A, Sinapis D, Sinapis A, Garway-Heath DF. Corneal biomechanical characteristics in patients with diabetes mellitus. *J Cataract Refract Surg* 2010;36(11):1822-1828
12 Alici S, Dulger HH. Nonenzymatic glycosylation of hemoglobins. *Van Tip Dergisi* 2001;8(3):105-110
13 Su DH, Wong TY, Wong WL, Saw SM, Tan DT, Shen SY, Loon SC, Foster PJ, Aung T, Singapore Malay Eye Study Group. Diabetes, hyperglycemia, and central corneal thickness: the Singapore Malay Eye Study. *Ophthalmology* 2008;115(6):964-968
14 Huntjens B, Charman WN, Workman H, Hosking SL, O'Donnell C. Short-term stability in refractive status despite large fluctuations in glucose levels in diabetes mellitus type 1 and 2. *PLoS One* 2012;7(12):e52947
15 Li HY, Luo GC, Guo J, Liang Z. Effects of glycemic control on refraction in diabetic patients. *Int J Ophthalmol* 2010;3(2):158-160
16 Sahin A, Bayer A, Ozge G, Mumcuoglu T. Corneal biomechanical changes in diabetes mellitus and their influence on intraocular pressure measurements. *Invest Ophthalmol Vis Sci* 2009;50(10):4597-4604
17 Scheler A, Spoerl E, Boehm AG. Effect of diabetes mellitus on corneal biomechanics and measurement of intraocular pressure. *Acta Ophthalmol* 2012;90(6):e447-451
18 Hwang YH, Kim HK, Sohn YH; Namil Study Group, Korean Glaucoma Society. Central corneal thickness in a Korean population: the Namil Study. *Invest Ophthalmol Vis Sci* 2012;53(11):6851-6855
19 Biswas S, Raman R, Koluthungan V, Sharma T. Intraocular pressure and its determinants in subjects with type 2 diabetes mellitus in India. *J Prev Med Public Health* 2011;44(4):157-166
20 Ko YC, Liu CJ, Hsu WM. Varying effects of corneal thickness on intraocular pressure measurements with different tonometers. *Eye* (*Lond*) 2005;19(3):327-332
21 Tonnu PA, Ho T, Newson T, El Sheikh A, Sharma K, White E, Bunce C, Garway-Heath D. The influence of central corneal thickness and age on intraocular pressure measured by pneumotonometry, non-contact tonometry, the Tono-Pen XL, and Goldmann applanation tonometry. *Br J Ophthalmol* 2005;89(7):851-854