ORIGINAL ARTICLE

Corneal endothelium count and thickness in diabetes mellitus

Rajesh Parekh, K. N. Ranganath, K. P. Suresh*, Mala Dharmalingam

Bhagwan Mahaveer Jain Hospital, *National Institute for Animal Physiology, Bangalore, India

AIM: To compare the endothelial structure and thickness of the cornea in diabetic and nondiabetic patients.

METHODOLOGY: The corneal endothelial cell structure and thickness of the cornea were evaluated using a specular microscope. One hundred and twenty-five eyes of 125 patients with diabetes mellitus (type 1 or type 2) were evaluated.The central corneal endothelial cell and thickness were also evaluated in 100 normal subjects. The correlation of the central corneal thickness and the grade of the diabetic retinopathy was investigated. Multivariate regression analysis was performed to assess systemic factors (patient age, sex, duration of diabetes, BUN, and creatinine values) and ocular factors (grade of diabetic retinopathy and history of laser treatment) related to the endothelial cell density.

RESULTS: The endothelial cell count was found to be significantly different in both diabetic groups, as compared with normal age-matched control groups. The central corneal thickness was also significantly different in diabetic patients who had undergone photocoagulation for diabetic retinopathy.

CONCLUSIONS: Corneal endothelial cell density and thickness is altered in diabetes. The alterations produced resemble those seen with ageing.

KEY WORDS: Cornea, diabetes, endothelium.

Introduction

Diabetes mellitus is perhaps the most important noninfective epidemic to hit the globe in the present millennium. Prevalence of diabetes in adults worldwide was estimated to be 4.0% in 1995 and to rise to 5.4% by the year 2025. Presently, it is higher in developed than in developing countries but by the year 2025, >75% of people with diabetes are estimated to be residing in developing countries, as compared with 62% in 1995.[1]

Diabetic eye disease is an end-organ response to the effects of the condition on the human system. Ocular morbidity results from major abnormalities of the retina and also by alterations in the eyelids, extraocular muscles, tear-film, cornea, iris, lens, and cranial nerves.

Corneal abnormalities in patients with diabetes have been demonstrated.[2–4] To the best of our knowledge, no paper has compared the corneal endothelial cell count (ECC) and thickness in an Indian diabetic population. Our study measures the ECC and thickness in a South Indian diabetic population.

Methodology

Subject selection

One hundred and twenty-five diabetic patients aged 18-72 years and 100 healthy age-matched controls participated in this study. Diabetic subjects (type 1 and type 2) were recruited randomly from those attending the Diabetes Clinic and Ophthalmology OPD of Bhagwan Mahaveer Jain Hospital and Netralaya, Bangalore. Diabetes mellitus was diagnosed on the basis of fasting blood sugar (FBS) level more than 140 mg/dl and postprandial blood sugar level of more than 200 mg/dl. Healthy controls were recruited from the staff and their relatives.

Informed consent was obtained from each subject. The

Correspondence to **Rajesh Parekh**, Maxvision Eye Care Centre, 25, Lavelle Road, Bangalore, India. E-mail: maxvision2020@yahoo.com

study protocol was approved by the Institutional Ethics and Review Committee. We excluded those subjects with any medical disease other than diabetes which required topical or systemic treatment that had known effects on any of the variables to be measured. We also excluded subjects with any intraocular surgery, current or past uveitis, and contact lens wearers. Pregnant and/or lactating women were also excluded from the study.

All subjects underwent a prestudy eye examination including ocular and medical history, visual acuity, and slit-lamp examination. Ophthalmoscopy was performed after dilatation of the pupil. The worse eye was used as the basis of stratification.

Five to ten central endothelial photographs of each eye were obtained on both eyes of all subjects with the TOPCON SP-20000P noncontact specular microscope, which also measured the central corneal thickness (CCT). The ECC and CCT were recorded.

Analysis of data

The data were assessed for normal distribution and were found to be normally distributed. Therefore, the parametric tests were applied for comparisons among the diabetic groups. The comparisons were made by performing ANOVA (*F*-test).The student's "*t*-test" was employed between healthy controls and diabetic subjects. Effect size was determined by the Cohen's "*d*" method.

Results

Descriptive data for the diabetics and healthy controls are shown in Tables 1 and 2. Forty percent of the study subjects were in the age group of 51-60 years. The study subjects had 60.8% males and forty four percent of the diabetics were type 2 diabetics [Tables 2].

Table 3 gives the cell density and thickness in the diabetic group and controls. The corneal cell density and thickness were different among the two groups. The endothelial cell density in both the diabetic and control groups showed a decrease over time, whereas the standard deviation increased [Table 4].

The duration of diabetes was significantly correlated with the cell density and the increase in thickness ($P<0.0001$). There was a significant relationship observed between the endothelial cell density, thickness, duration of diabetes, and the degree of microvascular complications (nephropathy–retinopathy). Those patients with severe retinopathy having undergone laser treatment showed a significant decrease in cell density and increased corneal thickness [Tables 5-8].

Table 1: Age distribution

Age group (years)	Diabetic (*n*=125)		Control (*n*=100)	
	No. of patients	%	No. of subjects	%
30 and less	6	4.8	11	11
31–40	11	8.8	14	14
41–50	20	16	24	24
51–60	50	40	34	34
61–70	31	24.8	16	16
>70 yrs	7	5.6	1	1

Table 2: Sex distribution

Sex	Diabetics (*n*=125)				Control (*n*=100)	
	No. of patients	Type 1	Type 2	%	No. of subjects	%
Male	76	21	55	60.8	70	70
Female	49	15	34	39.2	30	30

Table 3: ECC and corneal thickness in eyes of subjects with and without diabetes mellitus

	Mean ± SD	Student's *t*-test	Effect size
Diabetics			
ECC (cells/m^2)	2562.07 ± 35.98	6.640	0.89 (large)
Thickness (μm)	0.51 ± 0.03		
Control			
ECC (cells/m^2)	2852.27 ± 280.243	6.825	0.83
Thickness (μm)	0.51 ± 0.021		

Table 4: Distribution of corneal cell density, thickness, and standard deviation by age

Age (years)	ECC (cells/mm^2)	Corneal thickness (μm)
≤ 30	3113.76 ± 394.69	0.509 ± 0.022
31-40	2870.72 ± 284.3	0.517 ± 0.016
41-50	2818.39 ± 281.52	0.523 ± 0.023
51-60	2675.94 ± 261.38	0.529 ± 0.021
61-70	2433.30 ± 321.07	0.549 ± 0.029
>70	2203.88 ± 265.09	0.573 ± 0.021
	F = 22.427, P<0.001	F = 17.329, P<0.001

Discussion

The corneal endothelium plays an important role in the maintainance of the corneal transparency. The evaluation of the density and thickness of this layer is important in a wide range of disorders such as contact-lens-related complications, glaucoma, dry eye, and diabetes mellitus. The outcome of various intraocular surgeries including cataract, keratoplasty, vitrectomy, and refractive surgeries also rely on the status of the cornea.[2]

Table 5: Correlation of duration of diabetes and corneal morphology

Duration (years)	ECC (cells/mm^2)	Corneal thickness (μm)
<5	2724.75 ± 267.89	0.528 ± 0.018
5-7	2614.29 ± 302.61	0.537 ± 0.024
8-10	2428.12 ± 353.93	0.551 ± 0.021
>10	2082.68 ± 203.56	0.576 ± 0.024
	F = 26.930, P<0.0001	F = 26.374, P<0.0001

Table 6: Correlation of BUN and S. Creatinine levels with ECC (cells/mm^2) and corneal thickness (μm)

BUN	Normal range	>20 mg/dl	Student's "t"	Effect size
ECC	2667.72 ± 298.148	2196.07 ± 305.77	7.333	1.56
CCT	0.533 ± 0.022	0.569 ± 0.024	7.651	1.61
Serum creatinine	Normal	>1.5 mg/dl	Student's "t"	Effect size
ECC	2652.04 ± 308.59	2140.86 ± 261.87	7.225	1.76
CCT	0.534 ± 0.025	0.574 ± 0.019	7.78	1.87

Table 7: Severity of retinopathy, ECC and CCT

Retinopathy	ECC (cells/mm^2)	CCT (μm)
No retinopathy to mild	2748.79 ± 229.78	0.53 ± 0.02
Moderate to severe NPDR	2533.20 ± 338.35[a]	0.54 ± 0.03[a]
Proliferative DR/VH	2031.00 ± 95.09[b]	0.58 ± 0.01[b]
Significance	F=54.839F=52.520	
	P<0.001P<0.001	

VH- Vitreous Haemorrhage
[a]Significant in no or mild NPDR.
[b]Significant in moderate or severe NPDR.
ANOVA is used to find significance and Tukey test has been used post hoc to find the pairwise significance.

Table 8: Effect of laser on the corneal cell count and thickness

Laser	ECC (cells/mm^2)	Corneal thickness (μm)
No	2702.83 ± 262.67	0.53 ± 0.02
Yes	2051.19 ± 89.79	0.58 ± 0.02
Significance	t = 12.656, P<0.001	t = 11.676, P<0.001

Diabetes causes changes in the corneal endothelial cell morphology.[3] The corneal endothelium is known to demonstrate pleomorphism and polymegathism. We found a significant correlation of the endothelial cell density and the duration of the disease [Table 5], suggesting a cumulative effect of diabetes. These factors were also correlated with age [Table 4].

It is possible that morphologic changes with aging may be responsible for the decreased density and increased thickness of the cornea, as a significant correlation was also observed in the controls. Larsson *et al* also observed changes in the diabetic cornea, which were similar to that induced by aging.[3]

We found a significant relationship between endothelial cell density, thickness, and the severity of retinopathy [Table 7]. Weston *et al.*[4] found increased corneal thickness in diabetic patients. Yee *et al.*[5] also found endothelial changes in diabetic dogs similar to those of diabetic humans, with the degree of change positively correlating with long-term glycemic control. Saini and Mittal demonstrated significantly lower corneal endothelial function in patients with NIDDM but found that the state of glycemia, as indicated by FBS, did not play a role in endothelial dysfunction.[6]

In summary, we found an altered corneal endothelial cell density and thickness in subjects with diabetes mellitus, compared with controls. The values in the diabetic subjects matched those observed in aging. This study thus suggests a higher potential for the diabetic cornea to decompensate following any stress.

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