·Clinical Research·

Corneal changes in type II diabetes mellitus in Malaysia

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Abstract

• AIM: To compare corneal endothelial structure and central corneal thickness (CCT) between type II diabetics and non-diabetic control patients. To look for correlations between diabetic status and corneal findings.

• METHODS: Hospital-based, observational study. 200 eyes (from 100 type II diabetic patients and 100 controls) were included. Specular microscopy and pachymetry were used to measure endothelial cell density, size, coefficient of variation in cell area, hexagonality as well as corneal thickness. Independent t-tests were used to compare variables between diabetics and controls. Pearson correlation tests were used to evaluate correlations between corneal findings and diabetic status such as duration of diabetes, haemoglobin A1c (HbA1c) level and severity of diabetic retinopathy.

• RESULTS: Endothelial cell density in the diabetic group (2541.6± 516.4 cells/mm^2) was significantly lower than that in the control group (2660.1± 515.5 cells/mm^2, P<0.05). The average size of endothelial cells, standard deviation (SD) of cell size and coefficient of variation (CV) of cell area were all significantly higher in diabetics. Hexagonality was significantly lower in diabetics (41.1% ± 19.6%) compared to non-diabetics (45.2%± 20.6%). CCT was higher in diabetics but not significant (P>0.05). Duration of diabetes, HbA1c level and severity of diabetic retinopathy were not significantly correlated with corneal endothelial findings.

• CONCLUSION: Type II diabetes causes a significant alteration in the state of the cornea including reduction in endothelial cell density and increased pleomorphism and polymegathism. Central corneal thickness is unaffected.

• KEYWORDS: cornea; specular microscopy; type II diabetes mellitus; Malaysia

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INTRODUCTION

Type II diabetes mellitus is a major public health concern in this modern day. The International Diabetes Federation (IDF) estimated the global prevalence of diabetes to be 246 million in 2007 and possibly reaching up to 380 million by 2025. This translates into approximately 5.9% of the world adult population, with 80% of cases occurring in the developing world. South East Asian countries have the highest burden of diabetes. Data released by the IDF shows that Malaysia is one of the worst affected countries in Asia, with a prevalence of 9.9% and projected to rise up to 12.3% by the year 2025 [1,2].Diabetes mellitus can affect almost all structures of the eye. Patients can develop not only diabetic retinopathy but also corneal damage such as endothelial defects, punctate epithelial keratopathy, recurrent corneal erosions and persistent epithelial defects. Studies have also shown that corneal endothelial cells in diabetics have morphological abnormalities. These abnormalities include a decrease in endothelial cell density and hexagonality, as well as increased polymegathism, pleomorphism and CCT [3-6]. So far there has not been any published studies on the effect of diabetes mellitus on the corneas of diabetics in Malaysia. The purpose of this study was to investigate the effect of type II diabetes mellitus on corneal endothelial density, morphology and CCT by comparing these patients with normal subjects in a hospital population in Malaysia. We also looked to see if there were any correlations between the state of the cornea and other factors such as duration of diabetes, haemoglobin A1c (HbA1c) value and the stage of diabetic retinopathy.

MATERIALS AND METHODS

Materials Hospital-based, non-randomised observational study. All patients were from the University Malaya Medical Centre, Kuala Lumpur. This study was conducted over a one-year period from March 2006 to February 2007. It was approved by the Medical Ethics Committee of the University

Malaya Medical Centre, Kuala Lumpur and complied with principles of the Declaration of Helsinki. Patients aged 50 years and above who were diagnosed with type II diabetes were recruited. The diagnosis of type II diabetes mellitus was based on criteria of the World Health Organisation (WHO). Control patients were aged 50 years and above and did not have diabetes. In total, 200 patients were examined, 100 from each group. In this study, only the right eye of each patient was analysed. Exclusion criteria included active or previous eye infection or inflammation, glaucoma, previous ocular surgery or trauma, previous retinal photocoagulation, underlying corneal disease, pterygium, entropion, trichiasis, contact lens wear and regular usage of any eye drops or known tear-interfering systemic drugs (such as hormone replacement and anti-histamines). Patients with systemic illness known to impair tear function such as rheumatoid arthritis and systemic lupus erythematosus were also excluded.

Methods Informed consent was obtained from each participant. Age, gender, duration of diabetes, most recent HbA1c value, other medical illness and current medical treatment were recorded. Specular microscopy and pachymetry were then performed using a non-contact Topcon SP3000P (Topcon Corp, Tokyo, Japan) microscope. The captured image was analyzed with Topcon Cell Count software. Approximately 100 endothelial cells were counted in each image in the analysis. This was repeated three times for each eye and the image with the median number of endothelial cell density was used for analysis. Corneal endothelial cell density, size, standard deviation, coefficient of variation, hexagonality as well as CCT were measured. The pupils were subsequently dilated and fundus examination was performed by a single examiner. Retinopathy status was based on definitions from the Early Treatment of Diabetic Retinopathy Study (ETDRS) and classified into no diabetic retinopathy, non-proliferative diabetic retinopathy and proliferative diabetic retinopathy.

Statistical Analysis SPSS 12.0 (SPSS Inc, Chicago, USA) was used. Independent sample *t*-tests were used to compare the means between the diabetic and control groups. Pearson correlation tests were used to evaluate the association between corneal findings and demographic and clinical variables. For all the statistical tests, $P<0.05$ was taken as being significant. Values are shown as mean±SD.

RESULTS

The diabetic corneas have a significant increase in endothelial cell size (μm^2; 397.6±84.3 *vs* 380.0±80.4, $P<0.01$) and coefficient of variation (CV) (67.2%±47.2% *vs* 58.2%±43.0%, $P<0.01$). They also have reduced endothelial cell density (cells/mm^2; 2541.6±516.4 *vs* 2660.1±515.5, $P<0.01$) and hexagonality(41.1%±19.6% *vs* 45.2%±20.6%, $P<0.01$). There was no significant difference in CCT (μm^2; 517.3±53.4 *vs* 510.8±71.9, $P=0.149$). Pearson correlation analysis showed that duration of diabetes, HbA1c levels and severity of diabetic retinopathy had no significant correlations with corneal thickness, average size, SD of size, CV of size, hexagonality or endothelial cell density.

DISCUSSION

In this study, we found that type II diabetic patients showed a statistically significant reduction in mean corneal endothelial cell density of 4.5% compared to control subjects. This was similar to the 4.1% reduction found by Inoue *et al* [5] in their study of type II diabetics in Japan. Shenoy *et al* [3] in Oman and Lee *et al* [4] in Korea also reported significant reductions in endothelial density in their studies on diabetics and insulin dependant diabetics respectively. We also found that the average size and coefficient of variation (CV) of corneal endothelial cells to be significantly increased in diabetics. The increase in CV indicates the presence of polymegathism in which endothelial cells enlarge to fill the gaps between adjacent cells. Our study also showed that the percentage of hexagonal cells was significantly reduced in diabetic patients, indicating the presence of pleomorphism. These results were similar to those obtained by Lee *et al* [4] and Roszkowska *et al* [7]. However, Inoue *et al* [5] found that percentage of hexagonal cell to be not significantly different between diabetic and controls.

The presence of polymegathism, pleomorphism and reduction in density of corneal endothelial cells in type II diabetic patients clearly shows that diabetes affects the corneal endothelium. It is thought that intracellular accumulation of sorbitol, which acts as an osmotic agent leads to swelling of the endothelial cells. The Krebs cycle slows down with a consequent reduction in ATP production which is necessary for endothelial pump function. This eventually results in morphological and permeability changes in the corneas. There was no significant difference in CCT between diabetics and controls in our study. Our findings were similar to reported studies by Inoue *et al* [5] and Siribunkum *et al* [6].Other studies such as by Lee *et al* [4] and Roszkowska *et al* [7] reported a significant increase in CCT in diabetic patients. From our findings, we observed that the effect of Type II diabetes on the corneal thickness in this study population to be minimal.

Our corneal specular microscopy scans show that the corneal endothelium of diabetics attending our clinics are different

from non-diabetics. This difference may infer higher susceptibility to surgical stress and delayed healing following intraocular surgery, specifically cataract surgery. In order to study this, an on-going prospective study is being carried out presently on diabetic patients who are undergoing cataract surgery to compare with controls in our centre. As corneal specular microscopy data from South East Asian countries is scarce, we hope that ours can be used for future comparison with that from other studies from the region. In this study only type II diabetics were enrolled. Type I diabetics were not studied as the numbers were small among diabetics attending clinics at our hospital. As such, the effect of type I diabetes on the parameters mentioned previously was not studied.

In conclusion, corneal endothelial structure is affected by type II diabetes. Endothelial cell density is reduced and pleomorphism and polymegathism are increased. However, CCT is unaffected. Duration of diabetes, HbA1c levels and retinopathy status have no effect on endothelial structure. Routine assessment of corneal endothelial structure may be beneficial in all diabetic patients on top of their usual retinopathy assessment.

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