

Decrease of Corneal Sensitivity in Patients with Diabetes Mellitus Type II

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ABSTRACT

The aim of this study is to analyze decreasing corneal sensitivity in non insulin dependent diabetic patients. This study was cross sectional and performed in out-patient clinic Dr. Soetomo Hospital Surabaya from March until June 2009. Subjects were divided in 4 groups: without Diabetes Mellitus (DM), DM without retinopathy, DM with Non Proliferative Diabetic Retinopathy (NPDR), and DM with Proliferative Diabetic Retinopathy (PDR). Corneal sensitivity was measured using Cohcet Bonnet aesthesiometry. Retinopathy was recorded in fundal photograph. HbA1C level was measured to assess hyperglycemia control. Relationship of corneal sensitivity, diabetic retinopathy, and HbA1C level were analyzed using regression test. There were 42 patients enrolled in this study. Each group had 10 subjects (23.8%), except NPDR group had 12 subjects (28.57%). There was decreased corneal sensitivity in diabetic patients ($p_{RE} = 0.004$, $p_{LE} = 0.01$; regression test). In conclusion, there is influence of level of HbA1C in diabetes mellitus type II patients on decreased corneal sensitivity.

Key words: corneal sensitivity, HbA1C, diabetic retinopathy

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INTRODUCTION

Number of patients with diabetes mellitus in Indonesia every year tends to increase. Prevalence of diabetes in Indonesia ranges from 1.5% to 2.3%. Diabetes mellitus (DM) type 2 is a type of diabetes that includes more than 90% of the entire diabetic population, including those in Indonesia.¹ International Diabetic Federation (IDF) estimates that the total Indonesian population aged 20 years and over suffer from DM as many as 5.6 million people in 2001 and will rise to 8.2 million in 2020.²

Diabetes is a disease that has the most complications. This relates to the condition of persistent hyperglycemia, resulting in damage to blood vessels, nerves and other internal structure.^{1,3} To prevent chronic complications in patients with DM, it requires a good control of DM as a therapeutic target. Diabetes is well controlled if HbA1C level achieves the expected level of less than 7%. The higher the HbA1C, the higher the risk of diabetic complications. Skyler *et al.* reported a direct relationship between levels

of HbA1C with a relative risk of diabetic microvascular complications.⁴

Complications that occur in the eye may present as major abnormalities in the retina, changes in the eyelids, extra-ocular muscles, tear film, cornea, iris, lens and cranial nerves. Diabetes can affect every layer of the cornea. Corneal epithelium showed varying changes, including reduction in the number of cells, depletion and changes in basal membranes. In addition, to perform the function of protection, corneal nerve controls integrity, and proliferation of corneal epithelial wound healing.^{5,6}

The relationship between nerve damage and diabetes mellitus is currently focused mostly on the foot that causes development of the ulcer pedis and lower extremity amputations. Cornea is a much more sensitive organ, about 300–600 times more sensitive than skin. In patients with diabetes mellitus, corneal sensitivity is decreasing due to loss of corneal nerve fibers that cause keratopathy and more susceptible to injury, leading to susceptibility of recurrent erosion and ulcer.³ This study investigated whether the

decrease in corneal sensitivity in diabetes mellitus is associated with control of blood sugar levels.

The aim of the study was to analyze the reduction in corneal sensitivity and its relationship with the degree of diabetic hyperglycemia. It was expected to provide benefit in patients with DM, so they can be more alert and able to prevent eye complications that may arise and will hopefully obtain a practical method for screening examination so that the complications of blindness in individuals with diabetes can be prevented earlier.

METHODS

This study used cross sectional method, in patients with type II DM in Eye Outpatient Unit, Dr. Soetomo Hospital, in March–June 2009. Subjects were divided into 4 groups: control group (without diabetes mellitus), diabetes patients without diabetic retinopathy, diabetes patients with non-proliferative diabetic retinopathy, and diabetes patients with proliferative diabetic retinopathy. The total sample size of 42 patients were recruited using simple random sampling method. Criteria for inclusion of research subjects including age > 40 years, evaluable retina, never undergoing intraocular surgery, and no corneal abnormalities found (infection, cicatrix or corneal dystrophy). Corneal sensitivity served as dependent variables and levels of HbA1c as independent variables.

Patients with DM were confirmed by examination of fasting blood sugar 2 hours after eating, whereas good controls were evaluated by examination of their hyperglycemic HbA1C levels. Corneal sensitivity was checked using a Cochet-Bonnet aesthesiometer. Examination was conducted by gentle touching of Cochet-Bonnet filament nylon aesthesiometer on the central cornea and perpendicular (corneal central area is the most sensitive area). The normal value of corneal sensibility was obtained if the length of nylon was more than or equal to 55 millimeter.⁷ Examination of diabetic retinopathy used fundal photographs, and divided into three criteria: no diabetic retinopathy, non proliferative diabetic retinopathy and proliferative diabetic retinopathy. Data analysis used Kolmogorof Smirnov test for normality of data distribution. Differences of corneal sensitivity between groups were tested using regression test, and the interaction of diabetic retinopathy and HbA1c levels on decreased sensitivity to the cornea was analyzed using categorical regression test for not normally distributed data.

RESULTS

Research was conducted on 42 subjects of the study, 32 people suffering from diabetes mellitus and 10 people without diabetes mellitus as control.

Table 1 shows mean age of subjects were over 50 years, and female subjects outnumbered male subjects. Increasing

Table 1. Characteristics of subjects

Parameters	Without DM	DM-DR	DM+NPDR	DM+PDR
Age	52.50 ± 10.68	56.80 ± 8.74	56.33 ± 7.29	54.00 ± 5.77
Sex (male/female)	5 / 5	3 / 7	3 / 9	5 / 5
Length of DM (years)	0	5.00 ± 5.38	10.17 ± 5.31	7.60 ± 5.06
HbA1C	6.21 ± 2.37	5.83 ± 0.96	8.59 ± 2.35	8.04 ± 1.59
Right corneal sensitivity	5.90 ± 0.32	5.55 ± 0.60	4.79 ± 0.89	4.70 ± 0.71
Left corneal sensitivity	5.70 ± 0.48	5.20 ± 0.63	4.46 ± 1.12	4.85 ± 0.88
Right CCT	523.20 ± 36.56	536.90 ± 28.50	553.75 ± 35.05	552.30 ± 33.69
Left CCT	522.60 ± 33.70	534.30 ± 24.90	547.67 ± 30.07	551.40 ± 5.77

Notes:

Without diabetes: subjects are not suffering from Diabetes Mellitus

DM-DR: DM patients without Diabetic Retinopathy

NPDR + DM: DM patients with Non-proliferative Diabetic Retinopathy

DM + DM patients with PDR (Proliferative Diabetic Retinopathy)

CCT: Central Corneal Thickness.

Table 2. Mean corneal sensitivity in diabetes mellitus

Corneal sensitivity	DM-DR	DM+NPDR	DM+PDR
Right eye	5.55 ± 0.59 (n = 10)	4.79 ± 0.89 (n = 12)	4.70 ± 0.71 (n = 10)
Left eye	5.20 ± 0.63 (n = 10)	4.46 ± 1.12 (n = 12)	4.85 ± 0.88 (n = 10)

Notes:

DM-DR: DM patients without Diabetic Retinopathy

NPDR + DM: DM patients with Non-proliferative Diabetic Retinopathy

DM + DM patients with PDR Proliferative Diabetic Retinopathy

Table 3. The sensitivity of the cornea by HbA1C levels in each eye

HbA1C (%)	Corneal sensitivity								Total eye
	2.0 ri/le	3.0 ri/le	3.5 ri/le	4.0 ri/le	4.5 ri/le	5.0 ri/le	5.5 ri/le	6.0 ri/le	
< 6.5	- / -	- / -	- / -	- / 1	2 / 1	5 / 9	- / 1	15 / 10	44
6.5 – 8	- / -	- / -	1 / -	1 / 3	- / -	3 / 3	- / -	1 / -	12
>8	- / 1	1 / 1	- / -	4 / 4	- / -	6 / 4	1 / -	2 / 4	28

Note:

ri: right eye

le: left eye

age did not correlate with the degree of reduction in corneal sensitivity (Pearson correlation test, $p_{OD} = 0.188$, $p_{OS} = 0.068$). The mean length of suffering from diabetes in patients without diabetic retinopathy was 5 years, while those suffering from diabetic retinopathy had longer duration of DM. The length of DM was significantly correlated with corneal sensitivity (Pearson correlation test, $p < 0.001$).

HbA1C levels in diabetes mellitus patients with diabetic retinopathy was higher compared to diabetes mellitus patients without diabetic retinopathy. Decrease in corneal sensitivity occurred in diabetes mellitus patients with diabetic retinopathy. Central corneal thickness of diabetes mellitus patients with diabetic retinopathy was higher in comparison with control group.

There was a decrease in corneal sensitivity in patients who had diabetic retinopathy compared to those without diabetic retinopathy. As shown in table 2 from statistical analysis, diabetic retinopathy was significantly correlated with right-eye corneal sensitivity (Spearman's rho correlation test, $p = 0.014$), but did not correlate with the sensitivity of the left cornea (Spearman's rho correlation test, $p = 0.307$).

As main outcome, well controlled DM (HbA1C < 6.5%) had better corneal sensitivity and 59% (26 of 44 eyes) had corneal sensitivity equal or more than 5.5 mm (table 3). Subjects with poorly controlled diabetes mellitus (HbA1C levels > 8.0), the corneal sensitivity less than 5.5 mm was 75% (21 of 28 eyes). Statistical analysis obtained HbA1C levels affected the corneal sensitivity of the right and left eyes (regression test, $p_{RE} = 0.004$, $p_{LE} = 0.01$).

Diabetes mellitus patients with diabetic retinopathy generally had higher HbA1C levels compared with diabetic patients who had not suffered from diabetic retinopathy. From the statistical analysis was found that the degree of retinopathy had significant correlation with HbA1C levels ($p = 0.007$). There was significant influence (regression test, $p_{RE} = 0.005$, $p_{LE} = 0.049$) of HbA1C on corneal sensitivity of right and left eye.

DISCUSSION

Corneal sensitivity in patients with DM has decreased compared to normal people. This is due to decreased density

of nerve fibers in sub-basal layer of the cornea. In 1996, there was a publication on the use of corneal esthesiometry for diabetic retinopathy screening. In order to develop easy and valid screening procedure to determine the presence of diabetic retinopathy, the author observed changes in the cornea to predict the presence of diabetic retinopathy. The principle is that corneal hypoesthesia and diabetic retinopathy is caused by the same factor, i.e. the systemic disease and the first onset of both disorders tend to be simultaneous. Subsequently, the author searched for the possibility of easier diabetic retinopathy screening method or tools that can be handled by non-ophthalmologists.⁸

In a research by Touzeau et al. on the anterior segment of the eye, it was suggested that DM affects the transparency of the lens, the diameter of the pupil and corneal sensitivity.⁹ Along with research by Tavakoli et al. corneal sensitivity significantly reduced in diabetes mellitus patients compared to controls (4.31 ± 4.19 mm vs. 52.3 ± 9.7 mm, $p < 0.0001$), corneal sensitivity did not decrease in DM patients neuropathy ($p = 0.32$), but decreased significantly in DM patients with mild ($p = 0.01$), moderate ($p < 0.0001$) and severe ($p = 0.02$) neuropathy.³ In this study the sensitivity of the cornea in patients with DM decreased gradually, and the degree of decline seemed more severe along with increasing severity of the degree of diabetic retinopathy, although it was not statistically significant. There was graded reduction in corneal sensitivity with increasing age in both DM and non DM study subjects.³ In this study, increasing age in both DM and without DM group did not correlate with the degree of reduction in corneal sensitivity.

Minor changes in the degree of goblet cells and squamous metaplasia was found in patients with diabetic neuropathy and DM patients with peripheral neuropathy had decreased corneal sensitivity. This indicates that the corneal and conjunctival neuropathy is a manifestation of the eye due to distal diabetic neuropathy. Age and length of DM is also associated with decreased corneal sensitivity, where the age of 65 years or older have diabetic neuropathy percentage higher than patients aged less than 65 years (60.7%: 33.3%), and the length of DM of more than 15 years shows the percentage diabetic neuropathy higher than that less than 15 years.¹⁰ In this study, the duration of diabetes was correlated with corneal sensitivity.

A study by Parekh stated that corneal endothelial cell density and corneal thickness in patients with DM and controls differ between the two groups. Both these parameters decreased with age. The duration of diabetes was significantly related with increased cell density and corneal thickness. There was a significant correlation between endothelial cell density, corneal thickness, length of diabetes and the degree of microvascular complications (nephropathy and retinopathy). Changes in corneal endothelial cell density and corneal thickness in patients with diabetes mellitus were compared to that of control. The values in diabetic patients were consistent with the values in aging process. The study supports higher potential in DM patients for the occurrence of corneal decompensation after stress.¹¹

In patients with diabetes mellitus, vascular endothelium serves as cell barrier. Endothelium of the cornea also has the function as a barrier. If there is damage to endothelial cells, its function will be impaired, resulting in pump disorders and corneal hydration and there will be increase in corneal thickness and corneal sensitivity disorders. McNamara et al. emphasized the change of corneal structure in patients with diabetes mellitus. It is thought that hyperglycemia affects corneal hydration control so that it changes corneal thickness in diabetics mellitus.¹² Sonmez *et al.* argue that hyperglycemia is a major factor involved in the change of refraction in patients with DM and such changes are detected by the corneal keratometric topography.¹³ Weston et al. reported a decrease in diabetic corneal endothelial permeability during different levels of hypoxia. Some researchers explained that the trend of increased corneal thickness in patients with diabetes mellitus is due to pleomorphism and polymegathism compared to that the cornea of non-diabetics.¹⁵

CONCLUSION

Hyperglycemia control that marked by HbA1C influence the decrease of corneal sensitivity in diabetes mellitus patients. Well controlled had better corneal sensitivity. Diabetes mellitus patients with diabetic retinopathy generally had higher HbA1C levels compare to diabetic patients without diabetic retinopathy.

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