Early Differences in the Thicknesses of Peripapiller Retinal Nevre Fibre Layer (RNFL) in Patients withType 2 Diabetes Mellitus With no Diabetic Retinopathy

Diabetik Retinopatisi Olmayan Tip 2 Diabetli Hastaların Papilla Çevresi Sinir Lifleri Tabakasındaki Erken Değişiklikler

Utku LİMON[1]

ABSTRACT

Purpose: To examine the early differences in the thicknesses of peripapiller retinal nevre fibre layer (RNFL) by Stratus optical coherence tomography (OCT) in patients with type 2 diabetes mellitus with no diabetic retinopathy compared with normal control subjects.

Methods: OCT was performed on 60 eyes of 30 healthy nondiabetic patients (control group) whom did not have any ocular disease or other systemic disease and in 60 eyes of 30 type 2 diabetic patients but no opthalmoscopic evidence of diabetic retinopathy whom did not have any ocular disease or other systemic disease. The RNFL thickneses around the optic disc in superior, inferior, nasal and temporal areas were recorded.

Results: Age, intraocular pressure and refractive error that might affect the RNFL thickness were not statistically different among the groups. Mean nasal and superior RNFL thicknesses in patients with diabetes was significantly thinner than the control group (p=0.001, 0.015).

Conclusions: Early detection and treatment of DR is significant in diabetic patients to reduce the risk of blindness. Superior peripapiller RNFL thickness can be useful for detecting the earlyest changes of DR in patients with diabetes..

Key words: Makülar ödem, subtenon enjeksiyon

ÖZ

Amaç: Diabetik retinopatisi olmayan tip 2 diabetli hastaların papilla çevresi sinir lifleri (RNFL) tabakasında ki erken değişikliklerin Stratus optik koherans tomografi (OCT) ile saptanması ve normal sağlıklı grupla karşılaştırılması.

Materyal ve Metod: Başka hiçbir göz veya sistemik hastalığı olmayan 30 sağlıklı kişiden oluşan kontrol grubunun 60 gözü ile tip 2 diabeti olan ancak diabetik retinopatisi olmayan 30 hastanın 60 gözünün OCT leri alındı. Superior,inferior, nasal ve temporal kadranlarda ki peripapiller RNFL kalınlıkları kaydedildi.

Bulgular: Yaş, göz içi basıncı ve refraksiyon kusurları gibi RNFL kalınlığını etkileyen faktörlerde gruplar arasında anlamlı bir fark yoktu. Nasal ve superior kadranlardaki orlalama RNFL kalınlıkları diabeti olan hastalarda belirgin olarak ince idi(p=0.001, 0.015).

Tartışma: Diabetik hastalarda körlük riskini azaltmak için diabetik retinopatinin erken tanısı önemlidir. Diabetli hastalarda erken değişiklikleri saptamak için üst kadran RNFL değişiklikleri kullanılabilir.

Anahtar kelimeler: Makülar ödem, subtenon enjeksiyon

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Geliş Tarihi - Received: 01.08.2016
Kabul Tarihi - Accepted: 21.11.2016
Ret-Vit 2017;26:238-241

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INTRODUCTION

Diabetic retinopathy (DR) is the first cause of visual impairment and blindness in the adult working-age population.[1] Early detection of DR is important to prevent loss of vision in patients with diabetes mellitus.

The precise mechanisms to onset and progression of retinopathy remain.[2] For a long time, DR has been considered primarily a retinal microvascular disorder caused by the hyperglycemia. Nevertheless, some recent studies have demonstrated that retinal neurodegeneration is present before the development of clinically detectable microvascular damage.[3,4] Contrast sensitivity, colour vision, electrophysiological methods including electroretinography (ERG) and visual evoked potentials (VEP) show early abnormalities before the onset of the retinopathy.[5] Studies of the retinal nerve fiber layer (RNFL) have detected focal loss in diabetic patients.[6]

The purpose of this study is to determine effect of diabetes mellitus (DM) to peripapillary RNFL thickness by using spectral domain optical coherence tomography (OCT) in patients with type 2 DM with no DR compared with normal control subjects.

MATERIALS AND METHODS

Patients

Patients recruited from the opthalmology clinic of Ümraniye Education and Research Hospital (İstanbul-Turkey) between January 2015 and November 2015. I performed OCT on 60 eyes of 30 healthy nondiabetic patients (control group) whom did not have any ocular disease or other systemic disease and in 60 eyes of 30 diabetic patients but no opthalmoscopic evidence of diabetic retinopathy whom did not have any ocular disease or other systemic disease.

All patients underwent a complete opthalmic evaluation including best corrected Snellen visual acuity, anterior segment biomicroscopy, intraocular pressure measurement with Goldman aplanation tonometry, posterior segment biomicroscopy with a fundus lens The risk factors available (hypertension, hyperlipidemia, nephropathy, HbA1C, smoking, fasting blood sugar) for the development of diabetic retinopathy were recorded.

Patients were included if they had a diagnosis of type 2 DM and no DR. Same age group patients included ranging from 50 to 65 years old. Patients were excluded if they had the risk factors for development of diabetic retinopathy as hypertension, hyperlipidemia, nephropathy, smoking. Other excusion criteria were refractive errors more than ± 4 dioptrics, best corrected visual acuity below 0.8 decimal, glaucoma, previous ocular surgery, other ocular disease (posterior uveitis…) and systemic diseases that reduces RNFL such as multiple sklerozis, parkinson, alzaimer.

OCT Imaging

Optical coherence tomography was acquired through a dilated pupil by the same experinced examiner. The RNFL thickness was measured with optical coherence tomography using the Spectral OCT (Heidelberg Engineering, Heidelberg, Germany). A circular circumpapillary scan of 3.46 mm in diameter was applied by OCT to calculate RNFL thickness. The RNFL thickneses around the optic disc in superior,inferior,nasal and temporal areas were recorded.

Ethical Approval

The study was approved by the Ümraniye Education and Research Hospital ethical committe and performed according to the Helsinki declaration. Written informed consent was obtained from all participants.

Statistical Analysis

For statistical analysis MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba,Ostend,Belgium;2013) was used. A p value of <0.05 was regarded as significant. Descriptive statistics were used for to define continuous variables. Comparison of two independent and normal distributed continuous variables was performed with Student t test Two variables which do not fit the normal distribution was performed by Mann-Whitney U test.

RESULTS

Demographics

In first group 30 patients (8 male and 22 female) with type 2 diabetes were included. Averages ages were 56.48 (52-65) years, duration of average diabetes were 104.6 (12-240) months and average HbA1c % levels were 7.4 (5.4-11.6). 72% of patients were receiving oral anti-diabetic agents and 28% of them receiving daily insulin injectios. In control group 30 healthy nondiabetic patients (12 male and 18 female) included with an average age 55,27 years (53-65). Age, intraocular pressure and refractive error that might affect the RNFL thickness were not statistically different among the groups. No abnormality of optic disc appearance was detected, and cup-to disc ratio did not differ significantly among the groups (table-1).

RNFL thickness in diabetic patients

The differences in RNFL thicknesses between patients with type 2 diabetes and control group are given in table 2. Mean nasal and superior RNFL thicknesses in patients with diabetes were 80.3±14.3 and 115.4±17.2. Mean nasal and superior RNFL thicknesses in control group were 94.8±18 and 124.5±12. In diabetic group mean nasal and superior RNFL thicknesses were significantly thinner than the control group (p=0.001, 0.015). Other sectors mean RNFL thicknesses between two groups was not significant. Selective thinning of the RNFL was found in the superior and nasal quadrants.

Table 1:		
	Control	**Diabetic**
Patients, number	30	30
Mean age, yrs (SD)	55.27	56.48
Male / female (n)	8/22	12/18
Mean diabetes duration, yrs (SD)		8.7
Visual acuity, decimal (SD)	0.9	0.9
IOP, mmHG (SD)	15.3	16.8
SE, (SD)	0.46	0.42
Mean HbA1c%		7.4
C/D ratio	0.2±0.05	0.19±1.6

Table 2:			
Mean RNFl	**Control**	**Diabetic**	**P**
Superior	124.5±12	115.4±17.2	0.015
Inferior	135±18.6	131.6±19	0.372
Nazal	94.8±1.8	80.3±14.3	0.001
Tempora	77.1±10.5	73.8±11.8	0.243

Figure 1 illustrates cases of a 57 year old of healthy normal control and a 56 year old patient with diabetes with no diabetic retinopathy. Mean superior RNFL thickness was decreased in diabetic patient with no diabetic retinopathy.

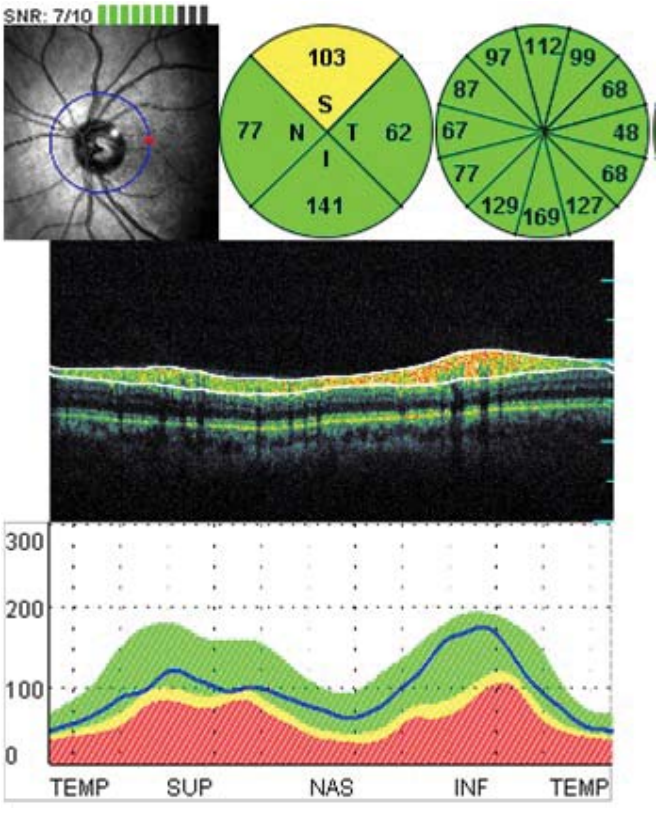

Figure 1:

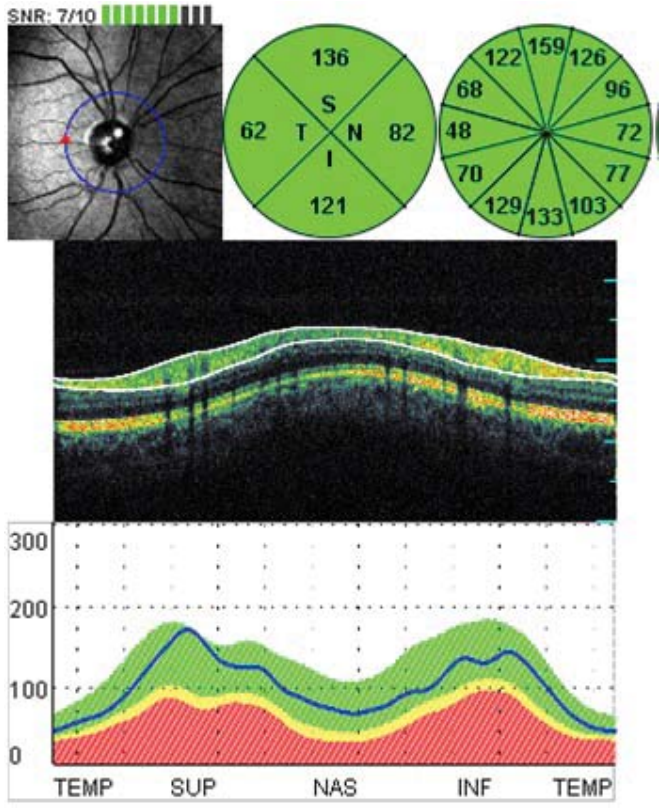

Figure 2:

DISCUSSION

Diabetic retinopathy is a retinal vacular lesion in patients with diabetes mellitus.[7] Still, there is some debate as to whether RNFL changes in diabetic eye are a result of the effect of vascular diabetic retinopathy or whether they are primarily caused by direct neurological damage after chronic hyperglycaemia.

Some reports suggest that neuronal dysfunction or neuropathy precedes the vascular abnormalities in the early stage of DM including apoptosis of retinal neuronal cells and activation of glial cells.[8] In diabetic animal models, damage of retinal neuronal cells and iner retinal thinning have been detected in the early stage of diabetic retinopathy.[9] Lopes et al demonstrated that diabetes associated RNFL loss develops before the onset of visible vascular retinopathy and RNFL thinning increases with disease severity.[10,11] Photographic evaluation of the RNFL in diabetic patients showed evidence of thinning.[12] RNFL thinning may possibly precede the detection of clinically visible lesions at the fundus. This may explain why there are early disruptions in vision such as reduction in contrast sensitivity before vascular lesions are detected at fundus.[13] This is why some reports suggest the usefulness of OCT for early detection of DR.[14]

In addition some reports suggest that diabetic retinopathy is manifested as vascular lesions. The potential cause of diabetes-associated RNFL loss is mainly explained by ischae-

mia, which caused by retinal vasculopathy. Takahashi et al demonstrated that RNFL defects were related to the severity of retinopathy.[15] This discrepancy may be the result of the posibility that pericyte deprivation leading to microaneurysm formation, microhemorrhages, ischemic damage and subsequent RNFL loss and peripapillary RNFL thinnig increases with disease severity.[16]

The current study, demonstrated a significant mean nasal and superior peripapiller RNFL thinning in patients with type 2 diabetes with no diabetic retinopathy. Other sectors mean RNFL thicknesses between two groups was not significant. Peripapiller RNFL thinning may possibly precede the detection of clinically visible lesions at the fundus. The neuronal abnormalities may explain the thinner peripapiller RNFL thickness if these developed before increased vascular permeability. There are many studies showing the superior RNFL thinning in the literature.[17,18] An animal model of diabetes showed twice the number of microaneurysms and cellular capillaries in the superior retina compared with the inferior retina.[18,19] Lower perfusion in the superior retina and the optic nerve head may cause greater ischaemia, retina ganglion cells and RNFL in the superior area may tend to be damaged structurally.[20] This observation may explain why the RNFL of the superior retina is more vulnerable to the metabolic stres of diabetes.

The objective determination of the RNFL thickness is essential. Determination of RNFL defects using scanning laser polarimetry (SLP) or OCT confirmed that thinnig is associated with the presence of diabetes mellitus.[21,22]

In conclusion, the findings of this study support the concept of DR as a neurodegenerative disease. Early detection and treatment of DR is significant in diabetic patients to reduce the risk of blindness. Superior peripapiller RNFL thickness can be useful for detecting the earlyest changes of DR in patients with diabetes. The detection of RNFL changes in diabetic patients with no diabetic retinopathy should offer new perspectives for understanding the mechanisms of DR. Multicenter studies with larger population are still necessary to assess RNFL thinning in diabetic patients.

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