



The Relationship between Central Macular Thickness and Metabolic Parameters Changes in Patients with Non-Proliferative Diabetic Retinopathy

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Abstract

Aim: To compare the directions changes in central macular thickness (CMT), glycosylated hemoglobin (HbA1c) and fasting serum lipids in patients with non-proliferative diabetic retinopathy (NPDR) along three-month follow-up.

Methods: Sixty-eight eyes of 68 patients with NPDR were included in this retrospective observational case series. CMT was measured using spectral domain optical coherence tomography at baseline and at third month follow-up visit. Fasting serum lipids including high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride (TG) and HbA1c levels were evaluated on the same day of CMT measurements. A potential relationship between HbA1c, serum lipids and CMT values were investigated by statistical methods.

Results: The mean age of the patients was 57.5 ± 9.8 years (38 - 80) and male-to-female ratio was 30/38 ($p > 0.05$). Along three-month follow-up period, CMT value increased in 31 eyes, decreased in 30 eyes and remained in the same level in 7 eyes. In the same period, HbA1c values increased in 39 patients and decreased in 22 patients and did not change the rest of them. The directions of changes in CMT and HbA1c were same for totally 41 patients ($p = 0.01$). These same directional changes were observed in totally 36 patients for CMT and HDL, in 23 patients for CMT and LDL, and in 28 patients for CMT and TG ($p > 0.05$, for all).

Conclusion: This study demonstrates the directions of changes in CMT and HbA1c levels were same; however, similar relationship was not observed for CMT and serum lipids including HDL, LDL, and TG along three-month follow-up in patients with NPDR.

Keywords: Central Macular Thickness; Diabetic Macular Edema; Diabetic Retinopathy; HbA1c; Lipid

Introduction

Diabetes mellitus is a chronic metabolic syndrome characterized by hyperglycemia due insulin resistance. Long-standing disease affects many organs and tissues causing several complications such as diabetic retinopathy and diabetic macular edema (DME). The pathogenesis of DME has not been exactly explained because complex processes with various contributing factors have been defined. Increasing diabetes duration with chronic hypergly-

cemia, advanced glycation end-products such as levels of glycosylated hemoglobin (HbA1c), free oxygen radicals, protein kinase C, hyperlipidemia, blood pressure play important role in this progressive metabolic disease. HbA1c is the index of average glycemic control over the previous 2 - 3 months and indicates the level of diabetic control; therefore, increased HbA1c concentration is the most important risk factor for developing diabetic complications mainly DME [1-6].

Optical coherence tomography (OCT) is a non-invasive highly reproducible imaging modality that visualize, *in vivo*, multiple thin slice, cross-section of biological tissues. It enables early visualization of intraretinal fluid accumulation that may not be seen on clinical fundus examination and central macular thickness (CMT) has been the most commonly used quantitative parameter for evaluation of macular edema [7-9].

Aim of the Study

The aim of this study is to investigate the relationship between CMT and HbA1c, and fasting serum lipids in patients with non-proliferative diabetic retinopathy (NPDR) by comparing the changes in their values.

Methods

This retrospective observational case series was carried out at the Ophthalmology Clinic of Ulucanlar Eye Research and Training Hospital with approval granted by the Local Research Ethics Committee (Ankara Numune Research and Education Hospital, 21.05.2014, E-14-200). All procedures were performed in accordance with the ethical standards of the Helsinki Declaration.

Right eyes of 68 Caucasian patients with NPDR (according to Early Treatment of Diabetic Retinopathy Study criteria) were included into this study. The exclusion criteria was as follows: 1) history or clinical findings of other retinal diseases (e.g. age-related macular dystrophy, retinal vein occlusion, retinitis pigmentosa, degenerative myopia, or uveitis); 2) history of previous retinal treatment (e.g. vitrectomy, intravitreal injection or implantation, or laser photocoagulation); and 3) media opacity (e.g. corneal opacity, dense cataract, or vitreous hemorrhage).

All patients were undergone detailed ophthalmic evaluation including visual acuity, intraocular pressure, anterior and posterior segment examinations. Spectral domain OCT (20 x 20 degree raster scans consisting of 49 horizontal high-resolution line sections) (Heidelberg Retina Angiograph-Optical Coherence Tomography, Heidelberg Engineering, Heidelberg, Germany) was used to evaluate CMT at baseline and at third-month of follow-up. HbA1c and fasting serum lipids including high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglyceride (TG) levels were determined at baseline and at third-month of follow-up via peripheral blood sampling. At baseline, an internal medicine consultation was

also performed for all patients to confirm presence of diabetes mellitus and to describe other systemic co-morbidities.

Statistical analyses of data were performed using with the Statistical Package for the Social Sciences software (SPSS Inc., Chicago, IL, USA) version 23. Descriptive statistics were expressed as mean and minimum-maximum. The normality of variables was assessed by Kolmogorov-Smirnov test. Wilcoxon test was used for comparison of each parameters measured in different examination period. In order to evaluate the correlation between changes of CMT, HbA1c and serum lipids chi-square test was performed. A p value < 0.05 was considered as statistically significant.

Results

The mean age of the patients was 57.5 ± 9.8 years (38 - 80). The male-to-female ratio were 30/38 ($p > 0.05$). A total of 44 (64.7%) patients had under insulin treatment while 24 (35.3%) had been receiving oral anti-diabetic medication. Any other diabetic complications such as polyneuropathy, nephropathy, or diabetic foot were not present in any of the patients. The most common systemic comorbidity was hypertension and it was observed in 28 (41.2%) patients out of 68 cases.

The mean CMT values were $290.0 \pm 48.9 \mu\text{m}$ (232 - 451) and $286.8 \pm 37.5 \mu\text{m}$ (241 - 403) at baseline and at third-month of follow-up. The mean HbA1c was $8.7 \pm 1.8\%$ (5.8 - 11.2) and $8.3 \pm 1.6\%$ (5.5 - 11.6) at baseline and at month 3. The mean values of HDL, LDL, and TG were $48.1 \pm 9.1 \text{ mmol/L}$ (29 - 87), $119.2 \pm 44.6 \text{ mmol/L}$ (43 - 294), and $165.6 \pm 52.5 \text{ mmol/L}$ (54 - 585) at baseline and $49.5 \pm 11.3 \text{ mmol/L}$ (30 - 82), $118.0 \pm 45.3 \text{ mmol/L}$ (49 - 284), and $159.5 \pm 47.4 \text{ mmol/L}$ (54 - 566) at third-month. There was no significant difference in CMT, HbA1c, and serum lipids between the values obtained at baseline and at third month ($p > 0.05$, for all).

Along three-month follow-up period, CMT value increased in 31 eyes, decreased in 30 eyes and did not changed in 7 eyes. In the same period, HbA1c values increased in 39 patients, decreased in 22 patients and remained in the same level in 7 case. The directions of changes in CMT and HbA1c were same for totally 41 patients and this relationship was statistically significant ($p = 0.01$). These same directional changes were observed in totally 36 patients for CMT and HDL, in 23 patients for CMT and LDL, and in 28 patients for CMT and TG ($p > 0.05$, for all). Table 1 summarizes the directions of changes in CMT, HbA1c, HDL, LDL, and TG values.

		CMT		p value
		Increased	Decreased	
HbA1c	Increased	25	14	0.01
	Decreased	6	16	
HDL	Increased	20	11	0.09
	Decreased	10	16	
LDL	Increased	12	17	0.15
	Decreased	19	11	
TG	Increased	13	15	0.70
	Decreased	18	15	

Table 1: The directions of changes in CMT, HbA1c, HDL, LDL, and TG values.

CMT: Central Macular Thickness; HbA1c: Glycosylated Hemoglobin; HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein; TG: Triglyceride.

Discussion

DME can occur at any stage of NPDR which limits patient functioning furthermore it remains a major cause of visual impairment and blindness [5,10]. Even diabetes mellitus is a complex disease and the risk of developing diabetic retinopathy was found to be associated with several factors such as increasing diabetes duration, HbA1c level, cardiovascular disease, and blood pressure [2,4-6]. In the current study, hypertension was found in 41.2% of patient which was the most common systemic co-morbidity in diabetic patients. Thapa, *et al.* [4] also found similar results with us that concurrent hypertension was observed in 55.7% and they observed that poor glycemic control (HbA1c > 7%) was found in 73.9% in newly diagnosed proliferative diabetic retinopathy among type 2 diabetes patients. Even this study investigates only patients with NPDR, the mean values of HbA1c were high and this finding shows that uncontrolled blood sugar is very common in patient with any stage of diabetic retinopathy.

According to different studies the higher the HbA1c level was higher the occurrence of DME. Jew, *et al.* [11] reported the correlation between HbA1c and DME in which the HbA1c was 7.8% in eyes without DME while it was 10.3% in the eyes with DME. Unsal, *et al.* [12] also found the average HbA1c level was higher in DME group

(9.0%) comparing to the NPDR group without DME (8.2%). According to the results of this study, the HbA1c levels were 8.7% and 8.3% in baseline and at month 3 respectively and the direction of change in CMT along three-month follow-up in patients with NPDR was similar with the direction of change in HbA1c and this result is highly consistent with the previous studies.

Several different researches showed that serum lipid profiles including total cholesterol, HDL, LDL and TG had not effect on CMT. Suwal, *et al.* [2] reported that poor glycemic control and high total cholesterol level had positive correlations with macular edema; however, there was no significant correlation between macular edema and HDL, LDL, and TG levels in their study group of 110 diabetic patients. In presenting study while absence of association with any type of fasting serum lipids and CMT changes, a significant correlation was observed between HbA1c and CMT changes in observation period. This result showed that long term blood sugar level is essential determining factor for macular edema.

The most important limitation of current study is short follow up period. The most strength of the study is using an alternative method to investigate the relationship between CMT, HbA1c, and fasting serum lipids in patients with NPDR. This study demonstrates the directions of changes in CMT and HbA1c levels were same; however, similar relationship was not observed for CMT and serum lipids including HDL, LDL, and TG along three-month follow-up.

Conclusion

This study demonstrates the directions of changes in CMT and HbA1c levels were same; however, similar relationship was not observed for CMT and serum lipids including HDL, LDL and TG along three-month follow-up in patients with NPDR.

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