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Original Research Article

Effect of anti-diabetic drugs on central macular thickness in patients with type 2 diabetes mellitus

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Abstract
Aim: To compare central macular thickness (CMT) of diabetic patients with type 2 diabetes without clinical retinopathy and healthy subjects.
Material & Methods: This is a prospective study, carried out on 92 patients. The patients were divided in to two groups: study group included 50 patients and control group comprised of 42 patients.
Results: The mean HbA1c level was 8.68 ± 2.39% in the study group and 5.10 ± 0.76% in the control group. The mean level of HbA1c was statistically higher in the study group than in the control group (Table 1, P = 0.001). Fasting plasma glucose level was statistically higher in the study group than in the control group (P= 0.001).
Conclusion: Central macular thickness was not significantly thicker in patients with type 2 diabetes without clinical retinopathy than in healthy subjects
Keywords: Central macular thickness, type 2 diabetes mellitus, retinopathy

Introduction

At least 171 million people worldwide suffer from diabetes and this is estimated to be doubled by 2030 (WHO2) [1]. Most common cause visual impairment in diabetic retinopathy (DR) is because of macular edema.
Optical Coherence Tomography (OCT) is a new investigative tool for quantification and classifying macular edema [2-3]. By measuring thickness it aids in early detection of macular edema and also in serial follow ups of patients on treatment. The mean macular thickness is large in all regions for eyes with Non-proliferative diabetic retinopathy (NPDR) or proliferative Diabetic Retinopathy (PDR) compared with the normal eyes. This difference is most significant in average and central foveal thickness [4].
Many factors are involved in DR development, such as blood pressure, hyperglycemia, diabetes duration, hypertension and HbA1c [5-7]. These factors may also be involved in macular thickness (MT) changes in diabetic patients and may be risk factors and even predictors of DME. The visual acuity (VA) of DR patients is often dependent on central foveal involvement, perifoveal capillary blood flow velocity and retinal thickness at the central fovea. DME has been reported to occur in 10% of DR patients [8-9]. Measuring MT in DM patients may lead to early detection of DR development and subsequent intervention. Optical coherence tomography (OCT) is an emerging technology used to perform cross-sectional imaging of the retina that can be used to measure MT [10].
Thus, we aim to compare central macular thickness (CMT) of diabetic patients with type 2 diabetes without clinical retinopathy and healthy subjects.

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Material & Methods

This is a prospective study, carried out on 92 patients. The patients were divided in to two groups: study group included 50 patients and control group comprised of 42 patients.

The central macular thickness (CMT) was measured in both groups by OCT (Optovue Inc. Co., RTVue 100 model, Fremont, CA, USA). The CMT was measured after providing pupil dilation with tropicamide drops 2 times, 10 minutes before measurements (Tropicamide 1%, Alcon Lab. Inc., USA). Three measurements were taken from each patient after pupillary dilatation. Blood biochemical tests for glycosylated hemoglobin (HbA1c) and fasting plasma glucose levels were run on all patients.

All cases underwent ophthalmological examinations including best corrected visual acuity (BCVA), anterior and posterior segment examinations under slit lamp, intraocular pressure (IOP) (applanation tonometer model AT 900, Haag-Streit, Switzerland), and central macular thickness measured by OCT. Visual acuity was measured with an early treatment diabetic retinopathy study chart at 4 meters. Each subject gave a written informed consent to participate in the study. The study adhered to the tenets of the Declaration of Helsinki.

Inclusion criteria for the study group included no visible findings of diabetic retinopathy (hard-soft exudates, microaneurysms) on retina at slit-lamp fundus examination with a +78 D lens, type 2 diabetes mellitus, no other problems (such as hypertension, uveitis) and no history of ophthalmologic trauma, intravitreal injection, high refractive errors (spherical equivalent between + 1.00 D and -1.00 D), or use of drugs(s) for retinal problems. Inclusion criteria for the control group patients included no ophthalmologic or systemic problems, no history of intraocular surgery or treatment of the retina, and no high refractive errors (spherical equivalent: between -1.0 D and +1.0 D).

Exclusion criteria for both groups were visible retinopathy or uveitis, hypertension, or previous ophthalmologic surgery. In the study group, the duration of diabetes mellitus ranged from 0 to 20 years and the average was 7.19 ± 4.87 years.

The Number Cruncher Statistical System (NCSS) 2007 and the PASS 2008 statistical software (Utah, USA) programs were used to evaluate the results of the study. Descriptive statistical methods (mean, standard deviation) and Student's t-test were used together to compare.

Results

The study group included 50 patients (100 eyes; 23 females, 27 males; mean age: 55.47 ± 11.73 years) who had type 2 diabetes mellitus without clinical retinopathy, and the control group included 42 patients (84 eyes; 28 females, 14 males; mean age: 55.38 ± 12.69 years) (Table 1). Best corrected visual acuity (BCVA) was 0.00 logMAR in both groups. No significant differences were found for the mean age, IOP, or gender distribution (Table 1).

The mean HbA1c level was 8.68 ± 2.39 % in the study group and 5.10 ± 0.76 % in the control group. The mean level of HbA1c was statistically higher in the study group than in the control group (Table 1, P = 0.001). Fasting plasma glucose level was statistically higher in the study group than in the control group (Table 1, P = 0.001).

In the study group, 3 patients were newly diagnosed, 17 patients were undergoing insulin treatment, and 6 patients were taking oral antidiabetic drugs (Table 2). Both groups were compared based on mean age, central macular thickness, fasting plasma glucose, and HbA1c levels.

No relationship was found between CMT and fasting plasma glucose level in the study (P = 0.582) and control (P = 0.399) groups. No relationship was found between CMT and HbA1c level in the study (P = 0.550) and control groups (P = 0.390; Table 3).

Table 1: Demographic characteristics, values for central macular thickness (CMT) and biochemical analysis in patients with type 2 diabetes without clinical retinopathy

Parameters	Study group (n = 50)	Control group (n = 42)	P
BCVA	0.00 (logMAR)	0.00 (logMAR)	NS
IOP mmHg	17.52 ± 2.6mmHg	18.1 ± 2.1 mmHg	NS

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Age (mean ± SD)	55.47 ± 11.73	55.38 ± 12.69	NS
Male/female	23/27	28/14	NS
CMT μm (±SD)	228.63 ± 23.61	217.72 ± 26.74	NS
HbA1c (mean ± SD)	8.68 ± 2.39	5.10 ± 0.76	0.001
Fasting blood glucose level			
Average	210.6 ± 108.7 (median: 170)	93.81 ± 7.60 (median: 94)	0.001

Table 2: Duration and treatment of diabetes mellitus in patients with type 2 diabetes without clinical retinopathy

Duration of DM	**(n = 50)**	**%**
New diagnosis	3	6
1-5 years	7	14
6-10 years	8	16
11-15 years	5	10
>15 years	4	8
Insulin treatment	17	34
OAD	6	12

Table 3: Relationship between central macular thickness (CMT), glycosylated hemoglobin (HbA1c), and fasting blood glucose levels in patients with type 2 diabetes without clinical retinopathy

Parameters	**Study group**		**Control group**	
	r	**P value**	***r***	**P value**
CMT-HbA1c	-0.082	0.582	0.001	0.390
CMT-fasting glucose	-0.094		0.011	

Discussion

In 2013, a study was done in Turkey also revealing decreased macular thickness in diabetics (227.19 ± 29.94 μm in healthy as compare to 232.12 ± 24.41 μm in diabetics) [11]. Murugesan S [12] and Jiang Jing *et al.* [13] also found decreased central macular thickness in clinically normal diabetic maculae in comparison to that of healthy individuals. Statistically significant pericentral retinal thinning has also been demonstrated by Biallosterski and co-workers [14], when they compared the retinal thicknesses of diabetics and healthy individuals, supporting the hypothesis of nerve tissue cell loss in the initial stages of diabetic retinopathy. In addition to this study by Nilsson *et al.* [15] also upholds our study result by demonstrating decreased retinal thickness in diabetic patients with early or no diabetic retinopathy.

Some studies have suggested that a high baseline HbA1c and a large reduction in HbA1c are risk factors for an increase in MT [16-17]. This may be because the pathogenesis of macular retinal thickening is not the same as the pathogenesis of hyperglycemia induced microangiopathy. There may be other unknown factors involved. Obesity has also been observed to have adverse effects on a variety of eye diseases. An increasing number of epidemiological studies have revealed a relationship between BMI and DR [18]. Elevated BMI is usually associated with hypertension and dyslipidemia, both of which are risk factors for DR [19]. However, we found no significant relationship between BMI and MT. This observation was consistent with the findings of previous studies [20]. Therefore, BMI may affect DR in many ways. A prolonged duration of diabetes has been thought to be a risk factor for DR [21-22]. This may be because prolonged exposure to the hyperglycemic state can increase the risk of vascular injury, leading to DR. Improving blood lipid status and controlling blood pressure with antihypertensive drugs can reduce the risk of DR progression [23-26].

Some of the previous studies have also glitazone [27-28] induced fluid retention with worsening of Diabetic Macular edema and its spontaneous improvement on withdrawal of this group of drugs. There was some contradiction in the scientific literature [29].

Yeung *et al.* [30], Chou *et al.* [31] and Rosenstock *et al.* [32] concluded that meticulous diabetes control may slow the progression of early diabetic retinopathy and may play an important role

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in preventing macular dysfunction. In type 1 and 2 diabetes patients, strict follow-up of plasma glucose level could reduce the progression and development of diabetic retinopathy.

Conclusion

Central macular thickness was not significantly thicker in patients with type 2 diabetes without clinical retinopathy than in healthy subjects. Our opinion is that the truly effective parameter on macular thickness is vascular permeability in patients with diabetes mellitus.

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