ORIGINAL RESEARCH PAPER

Ophthalmology

TO STUDY EARLY NEURO-RETINAL DEGENERATION IN TYPE 2 DIABETES & COMPARE IT WITH NORMAL SUBJECTS WITH SPECTRAL DOMAIN OCT

KEY WORDS: Spectral domain OCT, Diabetic retinopathy

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ABSTRACT

AIM: The aim of the following study is to evaluate the Central macular thickness (CMT), retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) thickness in patients with type 2 diabetes mellitus (DM) and compare it with normal subjects of same age groups..

MATERIALS AND METHODS: Central macular thickness (CMT), Retinal nerve fibre layer (RNFL) and Ganglion cell complex (GCC) thickness were measured in 180 eyes using spectral domain optical coherence tomography. The values of participants with DM were compared to controls. Diabetic patients were collected in Groups 1, 2 and 3. Group 1 = 50 eyes who had no diabetic retinopathy (DR); Group 2 = 50 eyes who had mild nonproliferative DR and Group 3 = 40 eyes who had moderate non-proliferative DR. The 40 healthy(non-diabetic) eyes collected in Group 4. Analysis of variance test used for statistical analysis.

RESULTS: The values of CMT, RNFL and GCC in the type 2 diabetes were thinner than controls and this difference was statistically significant.

CONCLUSIONS: This study showed that there is a significant loss of CMT, RNFL and GCC in patients with type 2 diabetes.

INTRODUCTION-

Diabetic Retinopathy (DR) is one of the most frequent causes of blindness in the working age population. Globally there is a rising trend in the prevalence of Diabetes Mellitus (DM) due to many factors such as increased life expectancy, urbani zation, increasing obesity, physical inactivity & genetics of Indian population .The international diabetes federation (IDF) predicts that the prevalence of DM in South East Asia will increase by two folds by the years of 2025.[1-4]

Diabetic retinopathy is a microangiopathy affecting the pre-capillary arterioles, capillaries and post- capillary venules which causes both microvascular occlusions and leakage .This microvascular occlusions leads to retinal ischaemia because of decrease oxygen support. Increased vascular permeability due to the breakdown of inner blood retinal barrier causes further changes of diabetic retinopathy with vascular changes, structural neurodegenerative changes such as neural apoptosis , loss of ganglion cell bodies glial reactivity & reduction of thickness of inner retinal layers .[8-12]

Recently Vascular endothelial growth factor (VEGF) is the most common target for treating diabetic macular ede ma(DME) and several other retinovascular diseases. But it is essential for neuroprotection because it reduces apoptosis of retinal ganglion cells.[13] Anti-VEGF agents causes reduction in VEGF level may cause neuro degeneration in diabetes. Therefore suspicion and detection of early signs of neuro degeneration could be beneficial in preventing vision loss in diabetic retinopathy.[14]

Recently Spectral domain OCT (SD-OCT) research has focused on the analysis of Retinal ganglion cell (RGCs) integrity in multiple sight-threateningdiseases such as glaucoma, optic neuropathies, and maculopathies.[15,16,17] SD-OCT is very much useful in diagnosing early neurodeg e neration by visualization of retinal layers & beneficial in preventing vision loss and deciding appropriate therapeutic approach in the management of diabetic retinopathy. The purpose of this study is to diagnose early neurodegeneration in type 2 diabetic patients with the help of spectral domain OCT.

AIMS & OBJECTIVES

1. Detect Early Neuroretinal degeneration by evaluating RNFL,GCC & Central macular thickness using SD- OCT in newly diagnosed type 2 diabetic patients.
2. Comparing the neuroretinal changes with healthy subjects of similar age group.

MATERIALS AND METHODS :

The proposed study was conducted in the Department of Ophthalmology, LLRM medical college, Meerut, India. All the newly diagnosed type 2 diabetic patients were recruited from OPD of ENDOCRINOLOGY department of our college & control from our OPD of OPTHALMOLOGY department. It's a CROSS-SECTIONAL study.

INCLUSION CRITERIA

in the study- All newly diagnosed TYPE 2 Diabetic partic I pants were included in this study from the opd of endocrine department & department of ophthalmology. Diabetic retinopathy, if present, will be classified as nonproliferative (no DR, MILD, MODERATE) & proliferative as per ETDRS classification .

EXCLUSION CRITERIA-

1. Severe NPDR
2. PDR
3. Presence of DME
4. History of any treatment for DR
5. Glaucoma
6. Uveitis
7. Significant media opacity,
8. Presence of any other retinal disease,
9. high myopia greater than −6 D or hyperopia greater than +3 D, and
10. history of retinal surgery.

A control group of healthy volunteers with no ocular or sys t emic disease eg: hypertension, diabetes and no high refractive error (more than −6 D or +3 D) will be included for comparision same age group & sex. After Complete Ophthal mologic examination of all diabetic patients including control ,Diabetic patients were divided into 3 groups. Groups 1, 2 and 3. Group 1 =50 eyes who have no diabetic retinopathy (DR); Group 2 = 50 eyes who have mild non proliferative DR and Group 3 = 40 eyes who have moderate non-proliferative DR. The healthy participants collected in Group 4 =40 eyes. OCT was done to diagnose early neuro retinal degeneration by evaluating CMT , Retinal neve fiber layer (RNFL),Ganglion cell complex(GCC) thickness of all type 2 diabetic participant's eye and control & data was compared. CMT, Average, inferior, and superior values of RNFL and GCC thickness were measured in 180 eyes using spectral domain optical coherence tomography. The values of participants with DM were compared to controls.Analysis of variance test analysis was used for statistical analysis.

OBSERVATION AND RESULTS

Table 1: MEAN CMT, MEAN RNFL, MEAN GCC

Parameters	Group1 Mean±SD	Group2 Mean±SD	Group3 Mean±SD	Group4 Mean±SD	P-value
CMT	213.52±5.77	209.12±7.30	209.55±4.61	226.9±5.07	<0.001
AVG.RNFL	115.92±6..4	106.52±10.34	114.52±4.85	124.4±3.90	<0.001
SUP.RNFL	95.70±13.44	97.54±5.31	101.65±5.74	113.75±3.12	<0.001
INF.RNFL	106.98±7.43	106.96±7.37	108.25±5.54	117.9±3.35	<0.001
AVG.GCC	107.60±4.55	106.88±4.86	117.48±3.86	120.96±2.01	<0.001
SUP.GCC	100.88±6.69	100.74±6.69	103.34±2.77	110.143±2.68	<0.001
INF.GCC	107.34±5.97	107.30±6.02	112.96±3.84	120.76±2.30	<0.001

Table 1- Showing thickness of CMT, RNFL, GCC in 4 groups. There is thinning of CMT, RNFL & GCC in diabetic patients compare to normal healthy subjects of same age group. The test is statistically significant (<0.001) .

DISCUSSION

This study was a cross-sectional study done in 180 eyes in which 50 eyes in diabetic with No-DR, 50 eyes in Mild NPDR, 40 eyes in Mod NPDR & 40 eyes in Normal healthy individuals of same age groups. For detecting Early Neuro-Reinal Degeneration CMT , RNFL & GCC were compared by SD-OCT in four groups. The morphological changes in various stages of DR are reflected by the differences in the retinal thickness in total or thickness of individual layers.

Yang *et al*[18] and **Forooghian *et al*[19]** have reported the changes in diabetic macular edema.Significant difference in retinal thickness was reported in various stages of DR using stratus OCT.Our group alsostudied the neuronal changes that occur in diabetic subjects who did not have clinical evidence of DR, Mild NPDR , Mod NPDR & Normal subjects. It was reported that SD-OCT measured CMT thickness was 213.52 μm in subjects with diabetes but no DR, 209.12 μm in MILD NPDR, 209.55 μm in MOD NPDR and 226.9 μm in non diabetic healthy subjects in table 4 & 5. In our study mean CMT is statistically significant.

Asefzadeh B*et al*[20] reported the correlationbetween macular thickness and diabetes control and duration. In subjects with no or mild DR, macular and foveal thickness is significantly thinnerwith longer duration of disease. This may reflect neurodegenerative changes in the diabetic retina.

Demir M *et al*[21] reported central macular thickness (CMT) of diabetic patients with type 2 diabetes without clinical retinopathy and healthy subjects. Optical coherence tomography (OCT) measurements were performed . No statistically significant relationship was found between CMT. Central macular thickness was not significantly thicker in patients with type 2 diabetes without clinical retinopathy than in healthy subjects. In my study RNFL & GCC were thinner in diabetic patients compared with same age group of healthy subjects & it was statiscally significant.

Mohammad A.M. *et al*[22] reported the effect of diabetic retinopathy (DR) on the retinal nerve fiber layer (RNFL) thickness. The global (G), the superior, and the temporal RNFL thickness in the diabetic patients without DR was significantly less than that of the control group and that of the patients with NPDR. However, there was no statistically significant difference between the patients with NPDR and the control group. It was noted that there was no statistically significant difference in the RNFL thickness of the inferior and nasal quadrants between the three studied groups. Early retinal neurodegeneration can occur before retinal micr ovascular diabetic changes can be observed.

Mehmet Demir*et al*[23]reported the retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) thickness in patients with type 2 diabetes mellitus(DM) .The values of RNFL and GCC in the type 2 diabetes were thinner than controls, but this difference was not statistically significant.). This study showed that there is a nonsignificant loss of RNFL and GCC in patients with type 2 diabetes.

Demir *etal.*[24] reported thinning of ganglion cells complex and RNFL in diabetic subjectts with various stages of NPDR, but with no statistically significant difference compared with healthy controls.

Lopes de Faria *et al.*[25] reported no significant difference in RNFL thickness in subjects with or without DR.

Carpineto P *et al*[26] reported that neuroretinal alterations in patients affected by type 2 diabetes with no diabetic retinopathy (DR) or mild nonproliferative diabetic retinopathy (NPDR) and without any sign of diabetic macular edema. Ganglion cell-inner plexiform layer (GC-IPL) and retinal nerve fiber layer (RNFL) thickness values were calculated after automated segmentation of SD-OCT scans. There was a significantly reduced GC-IPL and RNFL thickness values in both no-DR and mild-NPDR groups compared with healthy controls. These data confirmed neuroretinal alterations are early in diabetes, preceding microvascular damages.

Chiang PP *et al*[27] repoted that retinal ganglion cell (RGC) loss is present in subjects with diabetes and no DR, and is progressive in moderate or severe DR. RGC neuronal damage in diabetes and DR can be clinically detected using OCT.

CONCLUSION

In conclusion, early thinning on the retina starts in type 2 diabetes before visible vascular signs of DR.This supports the presence of a neurodegenerative process in eyes with diabetes and warrants for neuroprotective intervention to prevent chronic neurodegeneration. Early detection of neurodegeneration using SD-OCT may become indispe nsable for developing neuroprotection strategies in diabetic patients. So before starting Anti-VEGF it can be easy evaluate neuro degenerationSD-OCT evaluation of diabetic eyes helps to diagnose progression of the disease and needs to confirm the diabetic changes in retina. Correlation between structural changes in neural retina and functional change may expand the understanding of the early neurodegenerative process in diabetes.

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