The Professional Medical Journal
www.theprofesional.com

DOI: 10.29309/TPMJ/2019.26.09.3746

ORIGINAL PROF-0-3746

OPTICAL COHERENCE TOMOGRAPHY USE FOR ESTIMATION OF THE EFFICACY OF ANTI VEGF THERAPY IN DIABETIC RETINOPATHY AND DIABETIC MACULAR EDEMA.

Kanwal Ijaz[1], Muhammad Luqman Ali Bahoo[2], Beenish Karamat[3], Jamila Anwar[4]

1. MBBS, M.Phil. Physiology
   Senior Demonstrator
   Department of Physiology
   Fatima Memorial Medical and Dental College, Lahore.
2. MBBS, FCPS, FICO, FACS, Fellowship Refractive and Cornea Surgery
   Associate Professor & Head
   Department of Ophthalmology
   Shahida Islam Medical College, Lodhran.
3. MBBS
   Resident Medical Officer,
   Lahore general hospital.
   Lahore.
4. MBBS,MCPS Registrar
   Department of Ophthalmology
   Shahida Islam Medical College, Lodhran.

Correspondence Address:
Dr. Kanwal Ijaz
House No.507, Nargis Block, Allama Iqbal Town, Lahore.
drkanwal81@yahoo.com

Article received on:
21/05/2019
Accepted for publication:
28/07/2019
Received after proof reading:
28/08/2019

ABSTRACT… Objectives: To observe the role of optical coherence tomography in patients receiving anti-vascular endothelial growth factors for the treatment of diabetic retinopathy. **Study Design:** Observational descriptive study. **Setting:** The study was conducted at Department of Ophthalmology, Shahida Islam Teaching Hospital, Lodhran. **Period:** January 2018 to December 2018. **Material & Methods:** 177 eyes of 156 patients with diabetic retinopathy were analyzed with optical coherence tomography to quantify and explore changes in macula and inner retinal structures and to see different patterns of DME pre and post intra-vitreal anti-VEGF injections. All eyes had baseline OCT, received anti-VEGF intra-vitreal injection Avastin (Bevacizumab) 1.25mg/0.05ml. Follow up OCT imagining was done 6 weeks after last injection. **Results:** The patients had mean age of 58.36 ± 3.67 years with the mean diabetes duration of 9.30 ± 2.76 years. Before intra-vitreal injection, two different patterns of DME were recognized and analyzed i.e. diffuse thickening of macula (n=117, 66.10%) and cystoids macular edema (n=60, 33.90%). Base line OCT showed mean ± SD central foveal thickness 416 ± 54μm (n=177). On post intra-vitreal injection OCT, mean ± SD macular thickness was 212 ± 35 μm (n=177). **Conclusion:** OCT is latest non-invasive imaging modality that currently helps in quantifying and understanding the anatomy of DME and inner retinal damage due to diabetes mellitus. Although vascular leakage in DME is assessed qualitatively with Fluorescein angiography, actual macular thickness calculated with OCT is very helpful in yielding efficacy of treatment. This tool should always be used in monitoring the effect of therapies in future studies.

Key words: OCT, Anti-VEGF, DME Optical Coherence Tomography, Anti-vascular Endothelial Growth Factors, Diabetic Macular Edema.

Article Citation: Ijaz K, Bahoo MLA, Karamat B, Anwar J. Optical coherence tomography use for estimation of the efficacy of anti VEGF therapy in diabetic retinopathy and diabetic macular edema. Professional Med J 2019; 26(9):1506-1510. **DOI:** 10.29309/TPMJ/2019.26.09.3746

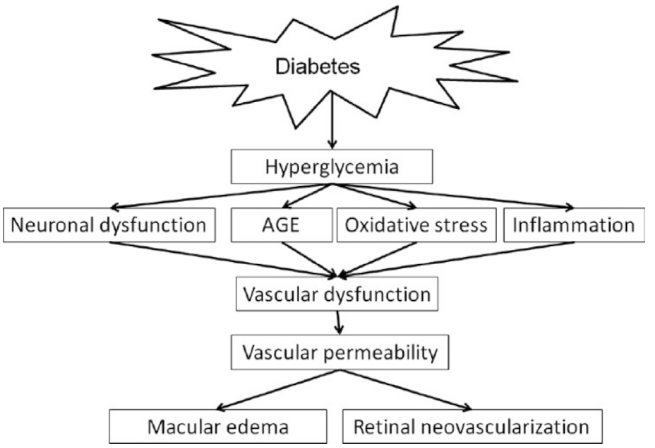
INTRODUCTION

Diabetes mellitus (DM) is globally widespread, presently affecting over 415 million peoples.[1] DM is among the very commonly prevailing disorders in Pakistan. 10 percent of total population of Pakistan is suffering from this disease making the Pakistan to be on seventh position in the world with large number of diabetic patients.[2] Marked hyperglycemia in DM is responsible for morbidity and mortality owing to its complications which either effect microvasculature such as in retina (retinopathy), in nerves (neuropathy) and in kidney (nephropathy) or effect macrovasculature leading to cerebrovascular accident, coronary heart disease and peripheral vascular disease.[3]

Diabetic retinopathy is commonly occurring, chronic microvascular problem of diabetic mellitus which causes the progressive vision loss worldwide.[4-5] Diabetic retinopathy (DR), the frequent origin of irreversible sightlessness in working-age population in developed world, effects the central vision and subsequently its demise occurring due to microvascular damage to the inner lining of the back of the eye, the retina.[6-7] The overall prevalence of any type of DR worldwide is 34.6%.[8] Previously, in Pakistan the occurrence of DR was reported at 26% but it has now progressed to 59%.[9] Almost 12 percent of diabetic having DR develops macular edema.[10]

High blood glucose levels cause biological and chemical alterations which results in vascular malfunctioning and porousness ultimately leading

to macular edema and retinal neovascularization.[11]



Pathophysiology of diabetic retinopathy

Different diagnostic approaches for DME are being employed. Slit-lamp bio microscopy of retina on which thickening of macula, presence of exudate or cystoid changes are appreciated. Fundus fluorescein angiography (FFA) reveals the zones of leaking retinal capillary. Optical coherence tomography (OCT) can display retinal section pictures, which enables the clinician to quantify the structural changes in the macula pre and post treatment.[12] It is a non-invasive diagnostic technique which utilize the infrared light rays with wavelength ranging from 800–840nm to yield high-resolution cross sectional image of the retina.[13]

Blood sugar levels, blood pressure and blood lipid profile should always be maintained within normal limits to prevent development and progression of DME as specified by American diabetic association.[14]

To treat DME, various treatment strategies like laser photocoagulation of retina, introduction of different pharmaceutical agents in vitreous, and vitreoretinal surgery are adopted.[12] The present study was designed to quantify the extent of DME pretreatment and change brought in the DME post treatment in patients who underwent anti VEGF intra-vitreal injection treatment.

METHODOLOGY

The observational descriptive study was carried out at Departments of Ophthalmology Shahida Islam Medical and Dental College, Lodhran from January 2018 to December 2018. This study was approved by local ethics committee of the hospital. Total 156 diagnosed diabetic patient, through purposive non-probability sampling were recruited only, if they consented to be the part of study. Type one and type two Diabetic patients of both genders (male and female) having diabetic macular edema and undergoing anti VEGF intra-vitreal injection, between the ages 30-80 years irrespective of duration of diabetes were included in the study. All diabetic patient having history of any ocular trauma or ocular surgery, presence of Cataract, glaucoma, and retinal detachment on slit lamp examination and ocular vascular diseases other than DR were excluded from the study. Pre-designed Performa were used to collect sociodemographic information (name, age, gender) of all the participants as well as to record observed findings pre and post treatment. 177 eyes with diabetic macular edema were analyzed with Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) machine to observe findings pretreatment with anti VEGF. Central foveal thickness greater than 220-280μm was considered edematous.[22] Total 177 eyes of 156 patients received anti-VEGF intra vitreal injections Avastin (Bevacizumab) 1.25mg/0.05ml twice with the interval of one month. Follow up OCT was done 6 weeks after last injection. The data was collected and analyzed using SPSS -17. The results were shown in frequency, percentages and mean.

RESULTS

In the present study, we included 156 diabetic patients received intra-vitreal injection of anti VEGF drug (Avastin; Bevacizumab 1.25mg/0.05ml). Out of these diabetic patients 135 (86.53 %) had unilateral diabetic retinopathy with macular edema while 21 (13.46%, Table-I) had bilateral diabetic retinopathy with macular edema. The incidence of type one diabetes was 30.12 (n=47) while incidence of type two diabetes was 69.87% (n=109, Table-II). The mean age of patients was 58.36± 3.67 years (Table-III). The mean duration of diabetes was 9.30 ± 2.76 years with the range of 4-18 years (Table-III).

Two different patterns of DME were recognized and analyzed before intra-vitreal injection: diffuse thickening of macula and cystoids macular edema. Out of 177 eyes of 156 patients 117 eyes (66.10%) displayed only diffuse thickness of macula while 60 eyes (33.90%) exhibit cystoid pattern of macular edema (Table-IV). 177 eyes of 156 patients, displayed mean macular thickness of 212 ± 35 μm on OCT after treatment with two (one month apart) intra-vitreal anti-VEGF injection from their base line mean central foveal thickness of 416 ± 54μm on OCT due to diabetic macular edema. (Table-V)

Eye Involvement	Frequency	Percentage
Unilateral macular edema	135	86.53%
Bilateral macular edema	21	13.46%

Table-I. Frequency of eye involvement (N=156)

Type of Diabetes	Frequency	Percentage
Type one diabetes	47	30.12%
Type two diabetes	109	69.87%

Table-II. Frequency of type of diabetes (N=156)

Study Variables	Mean ± SD
Age (years)	58.36 ± 3.67 years
Duration of diabetes (years)	9.30 ± 2.76 years

Table-III. Descriptive statistics (n=156)

Ocular Findings	Frequency	Percentage
Diffuse Macular thickness	117	66.10%
Cystoid macular edema	60	33.90%

Table-IV. Frequency of different ocular findings on OCT pre treatment (N=177)

Macular Thickness (μm)	Mean ± SD
Pre treatment	416 ± 54
Post treatment	212 ± 35

Table-V. Descriptive statistics of macular thickness pre and post treatment with anti-VEGF.

DISCUSSION

The microvascular complications like diabetic retinopathy lowers the quality of the life, imparting a great financial and social burden on suffering families and society, at larger, as well.[15] Recently the prevalence of DR in diabetic patients has been reported to be 28.78% in Pakistan.[16] Diabetic retinopathy can lead to development of diabetic macular edema which has threat to vision. Available and under research options for the treatment of DME include laser photocoagulation and intravitreal injection of pharmacological preparations like corticosteroid and anti-VEGF.[17] Among various diagnostic and prognostic tools, a relatively new and advance technique, OCT helps the clinician to quantify the structural changes of retina before and after treatment of DME.[12]

In our study the mean duration of diabetes was 9.30 ± 2.76 years with the range of 4-18 years. Another study reported the mean diabetes duration of 10.15 ± 3.2 years with a range of 4 years to 20 years.[18] Mason et al. reported the mean duration of diabetes of 18.4 years with a range of 3 years to 27 years.[19] Prolong duration of diabetes leads to development of diabetic maculopathy. Difference in Prevalence of DR has been reported in type one and type two diabetes.[18] In our study the incidence of type one diabetes was 30.12 (n=47) while incidence of type two diabetes was 69.87% (n=109) similarly in few other studies type two patients outnumbered the type one diabetes.[18-19] Contrary to it, study done by Arevalo et al reported the more prevalence of type one diabetes than type two diabetes among the patients suffering from diabetic macular edema.[20]

DME is usually diagnosed through contact and non-contact slit lamp biomicroscopy, indirect ophthalmoscopy, fluorescein angiography and fundus stereo photography. However, the diagnosis and management of DME has been revolutionized with advancement of OCT.[21]

With the help of OCT, clinician can understand, visualize the various pattern of DME more easily.[22-23] In our study we observed only two different patterns of DME i.e. diffuse macular thickness 66.10% and Cystoid macular edema33.90%. The study done by Trichonas et al, also reported the 95% prevalence of diffuse macular thickness in the study group. Various pattern that has also been observed in other studies includes diffuse retinal thickening (DRT), cystoid macular edema (CME) and serous retinal detachment (SRD).[22] Different classifications has

been proposed by different studies based on OCT findings.[22-23] Moreover, OCT enables the doctor to diagnose the DME early in its course through directly quantifying the extent of damage.[22,24]

The efficacy of treatment modality can also be evaluated and quantified better with the OCT scanning done prior and after the treatment.[24] We observed the reduction in macular thickness on the OCT images taken pre and post treatment of the eyes of the patients who received intra-vitreal injection of anti VEGF. The exact benefit of getting images of diseased retina with OCT pre and post treatment, is its quantifiable assessment, rather than the qualitative assessment as attained by other diagnostic techniques like biomicroscopy or fluorescein angiography.[25]

CONCLUSION

OCT is a novel non-invasive imaging technique which yields detailed image of retinal structural changes and patterns of DME along with quantification of damage, within a short time period and without giving much discomfort to the patients. Moreover it can be successfully utilized as a monitoring tool of the macular thickening before and after selected therapy.

REFERENCES

1. Siddiqui AA, Siddiqui SA, Ahmad S, Siddiqui S, Ahsan I, Sahu K. **Diabetes: mechanism, pathophysiology and management-A review.** Int. J. Drug Dev. & Res., 2013: 5(2):1-23.

2. **Diabetes statistics in Pakistan.** [Internet] 2013 Oct 5. [Cited July 6 2017]. Available from:<http://diabetespakistan.com/treatment/ABC-of-Diabetes/2013/10/05/diabetes-statistics-in-pakistan>.

3. Stratton IM, Adler AI, Neil HA, Mathews DR, Manley SE, Cull CA, et al. **Association of glycaemia with macro vascular and microvascular complications of type 2 diabetes (UKPDS 35): Prospective observational study.** BMJ. 2000 Aug; 321(7258):405-12.

4. Nentwich MM, Ulbig MW. **Diabetic retinopathy - ocular complications of diabetes mellitus.** World J Diabetes. 2015; 6(3):489–99. doi:10.4239/wjd.v6.i3.489

5. **Diabetic retinopathy guidelines, the royal college of ophthalmologists.** December 2012.

6. Lu Q, Lu P, Chen W, Lu L, Zheng Z. **ANGPTL-4induces diabetic retinal inflammation by activating Profilin-1.** Exp. eye res. 2018:166:140-50.

7. Das A, Stroud S, Mehta A, Rangasamy S. **New treatments for diabetic retinopathy.** Diabetes Obes. Metab., 2015:**17**(3): 219-30.

8. Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. **Global prevalence and major risk factors of diabetic retinopathy.** Diabetes Care. 2012; 35(3):556–64. doi:10.2337/dc11-1909.

9. Sohail M. **Prevalence of diabetic retinopathy among type -2 diabetes patients in Pakistan.** Pak. J. Ophthalmol.: 2014.30: 204-212

10. Paulus YM, Gariano RF. **Diabetic retinopathy: A growing concern in an aging population.** Geriatrics. 2009; 64 (2):16-20.

11. Shin ES, Sorenson CM, Sheibani N. **Diabetes and retinal vascular dysfunction.** J. Ophthalmic. Vis. Res., 2014:9:362-73.

12. Gundogan FC, Yolcu U, Akay F, Ilhan A, Ozge G, Uzun S. **Diabetic macular edema.** Pak J Med Sci. 2016; 32(2):505–10. doi:10.12669/pjms.322.8496.

13. Baskin DE. **Optical coherence tomography in diabetic macular edema.** Curr Opin Ophthalmol., May 2010; 21(3):172-77.

14. Breen EC. **VEGF in biological control.** J cell biochem 2007; 102:1358-67.

15. Stitt AW, Curtis TM, Chen M, Medina RJ, McKay GJ, Jenkins A et al. **The progress in understanding and treatment of diabetic retinopathy.** Prog. Retin. Eye Res., 2016; 51:156-86.

16. Mumtaz SN, Fahim MF, Arslan M, Shaikh SA, Kazi U, Memon MS. **Prevalence of diabetic retinopathy in Pakistan: A systematic review.** Pak J Med Sci. 2018; 34(2):493-500.

17. Akhtar HMU, Jandan NA, Diyal SM. **Effect of intravitreal bevacizumab for the treatment of diabetic macular edema.** PJMHS. July – Sep 2017; 11(3)1146-48.

18. Ateeq A, Tahir MA, Cheema A, Dahri A, Tareen S. **Intravitreal injection of Bevacizumab in diabetic macular edema.** Pak J Med Sci 2014; 30(6):1383-87.

19. Mason OJ, Yunker JJ, Vail R, McGwin G. **Intravitrealbevacizumab (Avastin) Prevention of panretinal Photocoagulation-induced complications in patients with severe proliferative diabetic retinopathy.** Retina. 2008; 28:1319-24.

20. Arevalo JF, Wu L, Sanchez JG, Maia M, Saravia MJ, Fernandez CF, et al. **Intravitreal bevacizumab (Avastin) for proliferative diabetic retinopathy: 6-months follow-up.** Eye. 2009; 23:117-123.

21. Fatima N, Qamar Ul Islam, Shafique M. **Frequency of vitreo macular traction in diabetic macular edema on optical coherence tomography.** Pak Armed Forces Med J. 2017; 67 (1):47-50.

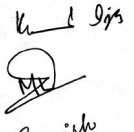
22. Trichonas G, Kaiser PK. **Optical coherence tomography imaging of macular oedema.** Br J Ophthalmol. 2014; 98 Suppl 2(Suppl 2):1124–29. doi:10.1136/bjophthalmol-2014-305305.

23. Gundogan FC, Yolcu U, Akay F, Ilhan A, Ozge G, Uzun S. **Diabetic macular edema.** Pak J Med Sci. 2016; 32(2):505-10.

24. Waheed NK, Duker JS. **OCT in the management of diabetic macular edema** Curr Ophthalmol Rep. 2013; 2013:1: 128.

25. Maalej A, Cheima W, Asma K, Riadh R, Salem G. **Optical coherence tomography for diabetic macular edema: early diagnosis, classification and quantitative assessment.** J Clinic Experiment Ophthalmol 2012; S2:004, doi:10.4172/2155-9570.S2-004.

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Kanwal Ijaz	Drafting of article, Interpretation of data, Critical revision of draft for important intellectual concepts.	
2	M. Luqman Ali Bahoo	Concept of study.	
3	Beenish Karamat	Literature search.	
4	Jamila Anwar	Data collection.	