Original article

Optical coherence tomographic assessment of macular thickness and morphological patterns in diabetic macular edema: Prognosis after modified grid photocoagulation

Shrestha A[1], Maharjan N[2], Shrestha A[3], Thapa R[4], Poudyal G[5]
[1]Geta Eye Hospital, Dhangadhi, Nepal, [2,4,5] Tilganga Institute of Ophthalmology, Kathmandu, Nepal,[3]Tribhuvan University, Institute of Medicine, Kathmandu, Nepal

Abstract

Introduction: The topographic mapping is useful for monitoring patients for the development of macular edema and following the resolution of edema after laser treatment.

Objectives: To evaluate the usefulness of optical coherence tomography (OCT) for mapping of macula after laser therapy in clinically significant macular edema (CSME).

Materials and methods: A prospective study was carried out enrolling 60 eyes of 35 patients with the diagnosis of CSME. OCT was performed at first visit and every successive follow up visit. The retinal thickness was measured automatically using OCT retinal mapping software. ***Statistics***: Correlation between vision status and central macular thickness (CMT) was done using the Spearman's correlation test. The analysis of variance (ANOVA) and independent t-test were used for comparison of groups.

Results: The OCT revealed sponge like thickening pattern (ST) in 67.4 % followed by cystoid macular edema (CME) in 19.6 %. Best corrected visual acuity (BCVA) improved in 89.1 % after 6 months of treatment. There was high correlation between vision status and CMT (P =<0.001). The mean values of baseline CMT were 301.68 (±134.738), 434.83 (±180.758), 518.67 (±275.184), 327 (±108.393) and 334.85 (±158.91) microns for the OCT patterns of ST, CME, sub-foveal detachment (SFD), vitreo-macular interface abnormality (VMIA) and average CMT respectively (p=0.042).

Conclusion: OCT is a useful tool for evaluating CSME. It can show the various morphological variants of CSME while the BCVA and CMT are fairly different.

Key-word: optical coherance tomography, central macular thickness, clinically significant macular edema, laser photocoagulation

Introduction

Macular edema is an important cause of visual loss and legal blindness in patients with diabetic retinopathy. In the Early Treatment Diabetic Retinopathy Study (ETDRS) focal laser photocoagulation was demonstrated to reduce the risk of moderate vision loss in CSME (ETDRS group, 1985).

OCT is a noninvasive imaging technique used to obtain high resolution cross-sectional images of the retina. It was not available at the time of the EDTRS study. The macular edema extent was determined by bio-microscopy examination or inspection of

Received on: 10.03.2011 Accepted on: 21.10.2011
Address for correspondence: Dr. Arjun Shretha, MD
Geta Eye Hospital, Dhangadhi, Nepal
Fax: 977 091 575112 Phone: 977 091 575112
Email: drarjuns@hotmail.com

stereoscopic photographs and was based only on the area of thickening, and not on the magnitude of the axial thickness. Variations in the amount of stereopsis present in paired stereo photographs or in the threshold for thickening adopted by the observer may further complicate the accurate and reproducible detection of areas of edema. Thus, there is potential for considerable variability and possible lack of sensitivity in prior art methods for identifying macular edema that were used in previous clinical studies (Virgili et al, 2007)

The topographic mapping protocol is useful for longitudinally monitoring patients for the development of macular edema and for following the resolution of edema after laser treatment. The false-color map of retinal thickness provides an intuitive and efficient method of comparing retinal thickness over several visits which could be directly compared with slit-lamp observation**.** OCT is a quantitative measure of CSME, unlike the other methods of detection. This technique operates on similar principles as ultrasound, but uses light waves instead of sound waves to detect ocular structures, allowing for a much higher (approximately 10 microns) resolution of images (Sony P et al, 2007).

Materials and methods

We enrolled 60 eyes of 34 patients with diagnoses of CSME in study between the August 2008 and July 2009. This was a prospective, non controlled, case series study done in Tilganga Institute of Ophthalmology (TIO), Kathmandu, Nepal. Patient had undergone modified grid photocoagulation with frequency doubled Nd: YAG laser at least once according to the ETDRS protocol. All patients were examined, which included BCVA measured with Snellen's charts, applanation tonometry, slit-lamp bio-microscopy, anterior segment evaluation and dilated fundus examination. At each follow-up visit, we assessed whether the patient had persistent, recurrent or new macular edema.

OCT was performed at first visit and every successive follow up visit with Stratus Zeiss Humphrey 2004 model. Quantitative OCT measurement namely retinal thickness was measured automatically using OCT retinal mapping software. CMT was defined as the mean retinal thickness in the circular zone of diameter 1 mm centered on the fovea.

Data collection

Especially designed Performa was used for the study. Hence the data pertaining to patient demographics, visual acuity, symptoms and signs, investigations, treatment modalities (Types of laser photocoagulation) and the outcome following laser therapy were collected.

Morphology

Different patterns of diabetic macular oedema by OCT are shown in figures. ST appears as diffusely thickened retina with areas of reduced intra-retinal reflectivity (fig 1), cystoids macular edema (CME) showing intra-retinal cystoid spaces (fig 2), SFD showing shallow elevation of the retina (fig 3), with an optically clear space between the retina and the retinal pigment epithelium and VMIA showing a highly reflective band over the inner retinal surface and extending towards the optic nerve or peripherally (fig 4).

Figure 1

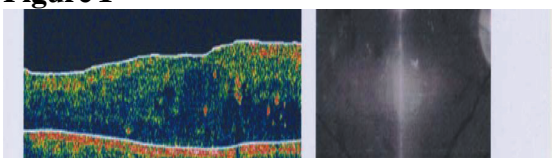


Figure 2

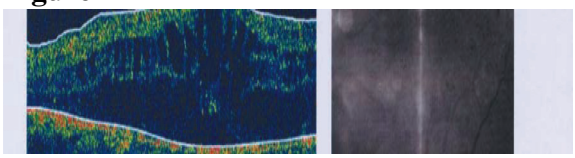


Figure 3

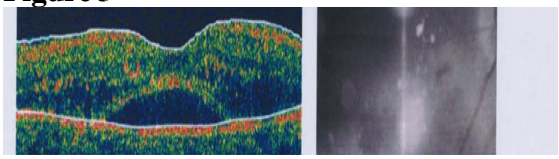
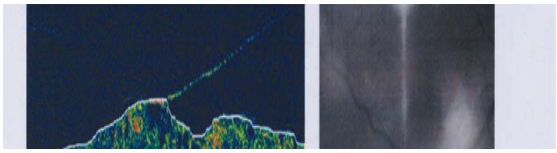


Figure 4



Our definition of ST allowed only pure ST. If ST and CME or SFD were combined, the classifications were CME or SFD, respectively; and when ST, CME and SFD were present, the classification was SFD. Regardless of pattern combinations, cases with epiretinal membrane (ERM) or vitreomacular traction (VMT) were classified as VMIA.

Statistics

Statistical analysis was performed with SPSS program (version 11.5). Data were expressed in frequency, percentage, mean and standard deviation as applicable. Correlation between vision status and CMT was done using the Spearman's correlation test. ANOVA was used to compare among groups and independent t-test was used to compare in each group. The p-value of less than 0.05 was taken as the level of significance.

To compare the visual outcomes of eyes with the four patterns, we defined at least all the letters what the patient was able to see or increments of BCVA by one line in the Snellen's chart as "improved," or decrement of letters even by one letter as "worsened" and other cases as "unchanged." This criterion was followed as mentioned by Zafar et al (2009).

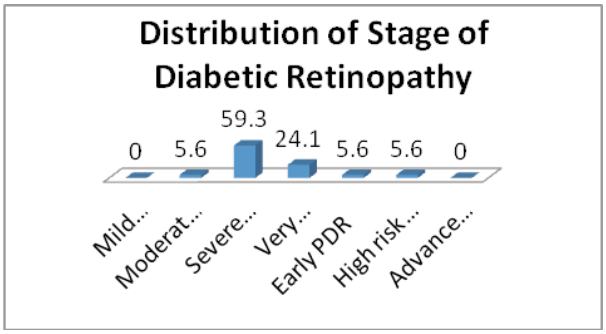
Results

60 eyes of 35 patients were enrolled in the study of which eight patients were lost for follow up. Therefore, only 46 eyes of 27 patients completed the study. Therefore, pre-laser analysis was done in 60 eyes while post laser analysis was done only in 46 eyes receiving laser treatment.

The mean duration of diabetes was 9.89 years and SD of 5.1 years. All the patients were of type II diabetes mellitus. 60 % of patients had the control of diabetes mellitus while 40 % of patients had no control of diabetes mellitus. Regarding the associated risk factors, 52 % had history of hypertension and were on treatment. Among them, blood pressure was controlled in 36 % and uncontrolled in 16 % with the medication.

Figure 5

Distribution of CSME in various stage of diabetic retinopathy (DR) by percentage



According to figure 5, majority of patients were in severe non-proliferative diabetic retinopathy (NPDR) group (59.3 %) followed by very severe NPDR group (24.1 %).

Table 1
OCT finding on 1st visit

OCT Morphology	%
ST	67.4
CME	19.6
ST+SFD	2.2
ST+VMIA	4.3
CME+SFD	2.2
CME+VMIA	4.3

The OCT revealed the ST pattern in 67.4 % followed by CME in 19.6 % (Table 1).

Table 2
Change in CMT from baseline

CMT in µm (Mean/SD)	ST	CME	SFD	VMIA	All	P- value
Baseline	301.68 (134.738)	434.83 (180.758)	518.67 (275.184)	327.0 (108.393)	334.85 (158.91)	0.042
6-month	284.67 (102.084)	372.57 (151.712)	462.50 (3.536)	401.25 (60.753)	315.91 (116.377)	0.019

The baseline CMT values (mean and SD) were 301.68 (134.738), 434.83 (180.758), 518.67 (275.184), 327 (108.393) and 334.85 (158.91) microns for ST, CME, SFD, VMIA and average CMT respectively and they were significantly different (p = 0.042 by ANOVA). The CMT was decreased in ST, CME and SFD but they were not statistically significant (p = 0.563, p = 0.513, p = 0.802) and this was significantly different between groups (p = 0.019). Similarly, at 6 months, the mean CMT measurements had decreased from 334.85 (158.91) to 315.91 (116.377), a difference that was also not statistically significant (p = 0.516).

Table 3
Visual outcome among eyes with laser treatment

Vision status	Month 1 (Number/ Percentage)	Month 3 (Number/ Percentage)	Month 6 (Number/ Percentage)
Improved / Static	34 (73.9)	38 (82.6)	41 (89.1)
Deteriorated	12 (26.1)	8 (17.4)	5 (10.9)
Total	46 (100)	46 (100)	46 (100)

Following laser, BCVA improved in 89.1 %, and deteriorated in 10.9 % after 6 month of treatment. There is a high correlation between vision status and central macular thickness (p=<0.001, Spearman's correlation test).

Discussion

Treatments for clinically significant macular edema include laser photocoagulation irrespective of stage of diabetic retinopathy. The OCT revealed ST pattern in 67.4 % followed by CME in 19.6 %. Rivellese M et al have also mentined the similar finding. Ferreira et al in 2007 found a different baseline incidence, with 57.5 % of scans demonstrating CME, 47.9 % ST and 20.5 % SRF. Two possible explanations were given for the discrepancy: first, this analysis only included patients with Diabetic macular edema (DME) who took the intra-vitreal triamcinolone injection and not just patients with DME, second; the data were collected using a newer version of OCT, with higher resolution.

BCVA improved in 15 eyes, remained static in 11 eyes and deteriorated in 4 eyes where blood sugar level was controlled and improved in only 9 eyes and remained static in 6 eyes where blood sugar level was not controlled in 6 months post laser. This signifies the importance of good glycemic control for better results following laser treatment. The United Kingdom prospective study has also confirmed that good glycemic control of type II, non-insulin dependent diabetes mellitus is beneficial and delays the onset of retinopathy (UKPDS, 1998).

In the follow up study of 214 surviving patients enrolled originally in Early Treatment Diabetic Retinopathy Study, 42 % had visual acuity of 20/20 or better and 84 % had visual acuity of 20/40 or better in better eye. Compared with baseline, 20 % had moderate vision loss (loss of 3 lines/more) in the better eye. Only 1 patient had visual acuity of 20/200 bilaterally (ETDRS, 1987).

In patients with diabetic retinopathy, laser treatment is directed at prevention of visual loss rather than visual improvement. Laser treatment usually does not cause an improvement in vision once it has decreased. In our study, we have included all cases with stable or at least one line improvement in VA as positive outcome. In our study, we followed the study definitions of ETDRS with respect to diagnosis and treatment of CSME. BCVA improved in 89.1 %, and deteriorated in 10.9 % after 6 months of treatment. There is a high correlation between vision status and central macular thickness (P value is <0.001 with Spearman's correlation test). This is almost similar to the study by Zaidi et al from Oman which showed that 29.7 % of patients maintained their baseline VA and 35.6 % of patients showed improvement in vision (Zafer et al, 2009). ETDRS showed that photocoagulation decreased persistent macular edema and significant visual loss by 50 % (ETDRS, 1985).

Laser photocoagulation remains the standard of care and the only treatment with proven efficacy according to a large-scale clinical trial. However, to our knowledge, the significance of patterns in terms of predicting response to focal laser photocoagulation has not been properly studied. In the present study,

the baseline CMT in mean and SD were 301.68 (134.738), 434.83 (180.758), 518.67 (275.184) and 327 (108.393) for different OCT patterns, ST, CME, SFD and VMIA respectively and they were significantly different (p=0.042). Similarly, the CMT was decreased in ST, CME and SFD but they were not statistically significant (p=0.563, p=0.513, p=0.802) and this was significantly different between groups (p=0.019). We hypothesize that this is explained by different CSME patterns.

Regardless of laser photocoagulation, one study found that VA is significantly better in ST eyes than in CME eyes (Yamamoto et al, 2001). Eyes with CME have been reported to respond poorly to modified grid laser photocoagulation. Chronic macular edema causes liquefaction necrosis of Müller cells, which forms cystoids cavities leading to CME. Cystoids spaces exist in the outer retinal layers initially but progressively extend to all retinal layers. It was reported recently that OCT-based retinal volumes and central macular thickness are equally effective at detecting CSME (Fine, Brucker, 1981). In the present study, we also found that retinal thickness can represent decreases in macular edema after focal laser photocoagulation. Data based on automatic measurement of third-generation OCT could decrease the precision of the data if the boundary lines were not properly assigned. Furthermore, the number of SFD and VMIA cases was small. We suggest that an understanding of structural changes evident by OCT in the macula of ST patients before laser photocoagulation would help predict treatment outcome. However, because of the limitations of the present study, a large prospective randomized controlled trial is required to investigate this relationship further.

There are also some shortcomings in this study. Glycosylated hemoglobin could not be done in every patient. Sample sizes for other morphological type except ST and CME were very few. We have not excluded patients from our study if grade 1 cataract had progressed to grade 2 according to LOCS 2 and this could have affected the final visual acuity, however if grade 3 cataract progressed to grade 4, they were excluded. Although, this 2nd generation OCT is very valuable in the context of developing country like Nepal, new generation OCT have already come in practice in other developed country. This will be replaced in future by new generation OCT.

Conclusion

OCT is a useful tool for evaluating CSME. It can show the various morphological variants of CSME while the BCVA and CMT are fairly different. Provided the availability of OCT in any eye institute, it will guide the treating ophthalmologist in a scientific way and remove the possible diagnostic dilemma.

References

Brasil OF, Smith SD, Galor A et al (2007). Predictive factors for short-term visual outcome coherence tomography study for diabetic macular oedema: an optical after intravitreal triamcinolone acetonide injection. Br J Ophthalmol; 91: 761-765.

Early Treatment Diabetic Retinopathy Research group (1985). Photocoagulation for diabetic macular edema: ETDRS report No 1, Arch Ophthalmology; 103:1796-806.

Early treatment Diabetic Retinopathy Study Research Group (1987).Technique for scatter and local photocoagulation treatment of diabetic retinopathy: Early diabetic retinopathy studyreport No. 3. Int Ophthalmol Clin; 27: 254-64.

Fine BS, Brucker AJ (1981). Macular edema and cystoid macular edema. Am J Ophthalmology; 92:466–81.

Rivellese M, George A, Sulkes D, Reichel E, Puliafito C (2002). Optical Coherence Tomography after Laser Photocoagulation for Clinically Significant Macular Edema. Ophthalmic Surgery and Lasers; 31 (13): 192-197.

Sony P, Venkatesh P, Garg S, Tewari H (2007). Step by step optical coherence tomography. Publisher – Jaypee Brothers, India; pages:15-18.

UK Prospective Diabetes Study Group

(1998). Turner R, Holman R, Stratton I et al. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes. BMJ; 317:703-13.

Virgili G, Menchini F, Dimastrogiovanni AF et al (2007). Optical coherence tomography versus stereoscopic fundus photography or bio-microscopy for diagnosing diabetic macular edema: A Systematic Review. Invest Ophthalmol Vi Sci; 48(11):4963-73.

Yamamoto S, Yamamoto T, Hayashi M, et al (2001). Morphological and functional analyses of diabetic macular edema by optical coherence tomography and multifocal electroretinograms. Graefes Arch Clin Exp Ophthalmol; 239:96–101.

Zaidi ZA, Jacob M (2009). Effect of macular photocoagulation on visual acuity of Omani patients with clinically significant macular edema. Oman Journal of Ophthalmology; 2:62-66.

Source of support: nil. Conflict of interest: none