

A study on laser photocoagulation in diabetic macular edema: Assessment with optical coherence tomography

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Abstract

Introduction: Diabetic macular edema (DME) is the most common cause of visual loss among diabetic patients. Macular photocoagulation is the established mode of treatment for clinically significant macular edema (CSME).

Objective: This study was conducted to know the response of focal and diffuse diabetic edema separately to frequency doubled Nd:YAG.

Materials and Methods: A prospective study with total of 30 consecutive eyes with Clinically Significant Macular Edema (CSME) over 8 months in our institution and divided into two groups with 15 each as focal and diffuse on the basis of fundus bio-microscopy and fluorescein angiography. Baseline measurements were done by OCT. Patients with diffuse diabetic macular edema underwent modified grid laser photocoagulation with Frequency Doubled Nd: YAG. Patients of focal diabetic macular edema underwent focal photocoagulation with Frequency Doubled Nd: YAG. Patients were followed up at 4 weeks and 12 weeks with repeat measurements by OCT with Humphrey Zeiss Stratus 3.0. Data entered in excel sheet and analyzed using SPSS software. The demographical data was analyzed with descriptive and the correlations by Pearson correlation.

Results: Among 15 eyes with focal macular edema mean age of patients was 59.80 ± 5.13 years whereas among diffuse macular edema, it was 67.80 ± 3.76 years. In the focal group, the mean BCVA letter score did not reveal a significant change at 4 and 12 weeks compared with the baseline ($p=0.52$ and $p=0.74$, respectively). In the diffuse group, the mean BCVA letter score showed a gradual decrease at 4 weeks and increased at 12 weeks compared with the baseline however this was not statistically significant. When central foveal thickness, perifoveal thickness, maximum retinal thickness and total macular volume were compared at baseline, 4 weeks and 12 weeks after surgery, it was found that visual outcome was better after laser photocoagulation in CSME when assessed using OCT.

Conclusion: Laser photocoagulation can be done for diabetic macular edema for better visual outcome and Optical Coherence Tomography (OCT) can give a quantitative assessment of the response of patients who have undergone focal and grid laser therapy.

Keywords: Diabetes, Macular edema, Laser Photocoagulation, Retinal thickness.

Introduction

Diabetic macular edema (DME) is the most common cause of visual loss among diabetic patients. Macular photocoagulation is the established mode of treatment for clinically significant macular edema (CSME) as defined by early treatment diabetic retinopathy study (ETDRS) group.¹⁻⁴ All eyes with CSME should be considered for photocoagulation.

a. **Direct treatment of focal fluorescein leaks:** Involves focal photocoagulation of individual microaneurysms. Goal is to obtain closure of the leak with preferred end point being whitening or darkening of microaneurysms. Spot size 50-200 μ .

b. **Grid treatment of diffuse edema:** Areas of retinal thickening and associated with areas of less intense leakage being treated with more widely spaced grid. The grid is not placed within 500 μ of the centre of the macula or within 500 μ of the disc margin, but it can be placed on the papillomacular bundle. The grid can extend in all directions up to 2 disc diameters from the centre of the macula. Spot size 50 – 200 μ .

c. **Modified grid laser treatment for diffuse edema:** Primarily involves grid treatment to areas of diffuse leakage with occasional treatment of focal leakage located within or outside the areas of diffuse edema. Modified grid is applied using 2/3 rows of 100 μ spots to all areas of perifoveal thickening up to and including the edge of foveal avascular

zone, these initial spots places 100 μ apart. Those, 150 – 200 μ spots are placed approximately 200 μ apart to the remaining areas of retinal thickening and capillary non perfusion. Focal leaks are treated with 100 – 150 μ spots to achieve mild whitening of microaneurysms.

Several large multi center studies have shown that laser photocoagulation reduces the macular edema in most patients and inhibits progression of vision loss in significant number of patients. However, there is limited information available regarding efficacy of macular laser treatment for CSME. However, no prospective trials had been conducted to know the response of focal and diffuse diabetic edema separately to frequency doubled Nd: YAG. This study was conducted to focus on the visual outcome of laser photocoagulation in CSME.

Materials and Methods

Materials: A prospective study was conducted among 30 consecutive patients with NPDR with CSME were recruited from our outpatient department over 8 months i.e June 2016 to January 2017 and they were divided into 2 groups, on the basis of fundus biomicroscopy and fluorescein angiography.

Group I: 15 eyes of focal diabetic edema

Group II: 15 eyes of diffuse diabetic edema

Inclusion criteria were patients with type II diabetes mellitus having NPDR with CSME on slit lamp biomicroscopy with 90D with focal / diffuse leak on

fluorescein angiography. Exclusion criteria were uncontrolled diabetes progressed to proliferative retinopathy, pregnancy, PDR, history of previous laser therapy, uncontrolled HTN, renal disease, patients with epiretinal membrane, pseudophakic macular edema and macular edema secondary to central or branch vein occlusion or any other diseases of the eye that can have an effect on vision like ARMD etc. Informed consent was obtained before inclusion and the study was performed in accordance with common ethical standards. A standard eye examination including best-corrected visual acuity (ETDRS chart), slit-lamp biomicroscopy (90-diopter [D] lens), clinical fundus photography, fluorescein angiography and retinal thickness with OCT was done. The blood level of glycosylated hemoglobin (HBA1c), FBS, PPBS was determined to assess the quality of blood sugar control. Patients with diffuse diabetic macular edema underwent modified grid laser photocoagulation with Frequency Doubled Nd: YAG. Patients of focal diabetic macular edema underwent focal photocoagulation with Frequency Doubled Nd: YAG.

OCT was performed at first visit and every successive follow up visit (4 and 12 weeks) with Humphrey Zeiss Stratus 3.0.

Methods

Data Collection: Specially designed Proforma was used for the study. The data pertaining to patient demographics, visual acuity, symptoms and signs, history of diabetes, investigations, treatment modalities (types of laser photocoagulation) and the outcome following laser therapy were collected

Follow up: Patients were followed up at 4 weeks and 12 weeks. At each follow up, visual acuity (bcva ETDRS chart), slit lamp biomicroscopy (with 90D), clinical fundus photography, fluorescein angiography and retinal thickness measurement with OCT was done.

Statistics: The data were entered in a Microsoft excel spreadsheet and analyzed using SPSS software. The demographical data was analyzed with descriptive and the correlations by Pearson correlation. The main effects of the repeated measures were analyzed on a general linear model, comparing with confidence interval adjustment being done by Bonferroni method.

Results

A total of 30 eyes of 15 patients with focal diabetic edema and 15 patients with diffuse diabetic edema were included in this study. Baseline demographic and clinical characteristics of both groups are summarized in Table 1.

Table 1: Baseline demographic and clinical characteristics of the focal and diffuse groups

Variables	Focal group	Diffuse group	p value
Age(years) (Mean, SD)	59.80 ± 5.13	67.80 ± 3.76	<0.001
Gender	Females	3	0.14
	Males	12	
BCVA (Mean, SD)	0.55 (0.27)	0.46 (0.35)	0.43
TMV (Cu.mm) (Mean, SD)	7.79 (1.32)	9.56 (3.077)	0.05
CFT±SD (μ) (Mean, SD)	275.33 (90.69)	375.53 (162.04)	0.04
Perifoveal thickness (μ) (Mean)	282	354	
Maximal RT (μ) (Mean, SD)	342.5 (84.47)	449.1 (169.16)	0.03

In the focal group, the mean VA letter score did not reveal a significant change at 4 and 12 weeks compared with the baseline ($p=0.52$ and $p=0.74$, respectively). In the diffuse group, the mean VA letter score showed a gradual decrease at 4 weeks and increased at 12 weeks compared with the baseline however this was not statistically significant. This may be due to compensation for the photocoagulation as a part of body response. The decrease in mean central foveal thickness in diffuse group at 4 weeks was 4.6% and at 12weeks was 18%. There was no statistically significant change in mean central foveal thickness at 4 weeks with the P value at 4 weeks being 1.00 and at 12 weeks being 0.06. (Table 2)

The average thickness in all the areas of all the patients was computed and the perifoveal thickness was calculated

by adding all the 8 areas other than the central fovea. The increase in mean perifoveal thickness in focal group at 4 weeks was 3.1% and at 12 weeks was 0.7%. Change in the mean perifoveal thickness was not significant statistically with P value at 4 weeks being 0.394 and at 12 weeks being 1. The decrease in mean perifoveal thickness in diffuse group at 4 weeks was 6.4% and at 12 weeks was 12.9%. There was no statistically significant change in mean perifoveal thickness at 4 weeks with P value at 4 weeks being 1.00 and at 12 weeks being 0.06. (Table 2)

The area of maximum retinal thickness in each patient was noted and the changes in that same area were noted after 4 weeks and 12 weeks after laser therapy. The decrease in the mean thickness in focal group at 4 weeks was 1.14% and at 12 weeks was 7.4%. The change in mean thickness in

the area of maximum retinal thickness was not statistically significant with P value at 4 weeks being 1.00 and at 12 weeks being 0.677. The decrease in mean thickness in area of maximum retinal thickness in diffuse group at 4 weeks was 12.8% and at 12 weeks was 22%. The change in mean thickness in the area of maximum retinal thickness at 4 weeks was not statistically significant. The change in mean thickness in the area of maximum retinal thickness was significant at 12 weeks with the P value at 4 weeks being 0.135 and at 12 weeks being 0.018. (Table 2)

There was no change in mean total macular volume in focal group at 4 weeks. However at 12 weeks there was a decrease in total macular at 12 weeks by 2.6%. The change in mean total macular volume was not statistically significant with P value for 4 weeks being 1.0 and P value for 12 weeks being 1.0. The decrease in mean total macular volume in diffuse group at 4 weeks was 7.3% and at 12 weeks was 11.2%. The change in mean total macular volume was not statistically significant with P value at 4 weeks being 0.281 and 12 weeks being 0.89. (Table 2)

Table 2: Mean change in different variables at follow-up visits in the two groups

Variable	Follow Up Visit	Focal Group Mean (SD)	P value	Diffuse Group Mean (SD)	P value
BCVA	Baseline	0.55 (0.27)	-	0.46 (0.35)	-
	4 Weeks	0.58 (0.3)	0.52	0.42 (0.35)	1
	12 Weeks	0.69 (0.31)	0.74	0.48 (0.37)	1
TMV (Cu.mm)	Baseline	7.79 (1.32)	-	9.56 (3.077)	-
	4 Weeks	7.82 (1.36)	1	8.86 (2.1)	0.281
	12 Weeks	7.63 (1.55)	1	8.48 (2.08)	0.89
CFT±SD (microns)	Baseline	275.33 (90.69)	-	375.53 (162.04)	-
	4 Weeks	298.2 (113.7)	0.281	362.47 (146.1)	1
	12 Weeks	296.13 (125.84)	0.960	306.93 (127.9)	0.06
Perifoveal thickness (microns)	Baseline	282	-	354	-
	4 Weeks	291	0.394	331	1
	12 Weeks	284	1	308	0.06
Maximal RT (microns)	Baseline	342.5 (84.47)	-	449.1 (169.16)	-
	4 Weeks	338.5 (116.9)	1	392.4 (141.25)	0.135
	12 Weeks	322.1 (80.8)	0.677	350.53 (117.53)	0.018

Discussion

CSME has been described by ETDRS studies and divided into three groups: type 1, type 2 and type 3. Type 1 includes the center-involving ME, whereas type 2 and type 3 represent the non-CI ME types. Modified ETDRS (mETDRS) focal/grid laser photocoagulation protocol in center-involving ME, adopted from the original ETDRS, is the widely used technique by most retinal specialists.⁵

In our study, the decrease in the mean thickness in focal group at 4 weeks was 1.14% and at 12 weeks was 7.4%. The change in mean thickness in the area of maximum retinal thickness was not statistically significant with P value at 4 weeks being 1.00 and at 12 weeks being 0.677 whereas in a DRCR.net study evaluating macular photocoagulation regimens demonstrated that the mETDRS laser approach was more effective in reducing retinal thickening at 12 months than a mild macular grid laser technique.⁶

Change in Mean Central Foveal Thickness

Diffuse Group: In our study, we found that the central foveal thickness in the patients who underwent grid laser photocoagulation, the central foveal thickness at baseline was 376 μ and following laser therapy decreased to 368 μ at 1 month and 307 μ at 3 months, corresponding to decrease in mean central foveal thickness by 4.6% and 18% respectively. In the study by Masahiko Shimura et al,⁷ there was a decrease in the mean central foveal thickness with

thickness before laser therapy being 534.7 \pm 120 μ and that after 6 Months of laser therapy found to be 286.9 \pm 98.6 μ , which corresponded to a decrease of 45.4% \pm 17.1%

Focal group: In our study, we found that the central foveal thickness was 275 μ prior to laser treatment and 298 μ and 296 μ at 1 and 3 months after laser therapy. This corresponds to an increase of 8.36% and 7.36% respectively. In focal group (n=12), the mean central foveal thickness was 258 μ prior to laser Photocoagulation and 264 μ and 244 μ , 1 and 3 months after laser therapy. This corresponds to an initial increase by 2.3% and then a decrease by 5.4% respectively. In the study by Laursen M L et al,⁸ the central foveal thickness at baseline in patients who underwent focal laser photocoagulation with diode laser was 275 \pm 93 μ and post treatment central foveal thickness was 250=77 μ at 3 months and 256 \pm 62 μ at the end of 6 months, corresponding to a decrease of 9% and 7% from baseline respectively. In the argon laser group that underwent focal laser therapy, the central foveal thickness prior to laser photocoagulation was 325 \pm 74 μ and post laser treatment central foveal thickness was 317 \pm 33 μ at 3 Months and 305 + 16 μ corresponding to an increase of 1% and a decrease of 3% respectively from the baseline.

Change in mean perifoveal thickness (average of all 8 areas apart from central fovea)

Diffuse group: In our study, the perifoveal thickness at baseline was 354 μ and following laser therapy decreased to

331 μ at 1 month and 308 μ at 3 months, corresponding to decrease in mean central foveal thickness by 6.4% and 12.9% respectively. Laursen M L et al⁸ noted that in patients, who underwent grid laser photocoagulation by diode laser, the perifoveal thickness at baseline was $309 \pm 29 \mu$ and following laser therapy, the perifoveal thickness was $306 \pm 28 \mu$ and $295 \pm 14 \mu$ at 3 and 6 months respectively. This corresponds to decrease in the thickness by 1% and 5% respectively.

Focal group: In our study, the perifoveal thickness was 282 μ prior to laser treatment and 291 μ and 284 μ , 1 and 3 months after laser therapy. This corresponded to an increase of 3.1% and 0.7% respectively. In focal group (n=12), the mean perifoveal thickness was 273 μ prior to laser photocoagulation and 274 μ and 261 μ , 1 and 3 months after laser therapy. This corresponds to an initial increase by 0.3% and then a decrease by 4.3% respectively. Laursen ML et al⁸ noticed that in patients who underwent focal laser therapy with diode laser had a perifoveal thickness of $333 \pm 68 \mu$ prior to laser photocoagulation and $317 \pm 65 \mu$ and $298 \pm 58 \mu$ 3 and 6 months following laser therapy, corresponding to a decrease in 5% and 10% respectively. However in patients who underwent focal laser photocoagulation with argon laser, in the same study, had a baseline perifoveal thickness of $315 \pm 41 \mu$ and following laser therapy this increased to 317 μ months and decreased to $305 \pm 16 \mu$ at 6 months. This corresponds to an increase in 1% and decrease in 3% respectively.

Change in total Macular Volume

This was another approach, not done by previous studies, in which we noted the change in the total macular volume. In patients who underwent focal laser therapy, the mean total macular volume prior to laser photocoagulation was 7.83 cubic mm and following laser therapy was 7.83 cubic mm and 7.63 cubic mm at 1 month and 3 months, corresponding to decrease of 0% and 2.6% respectively. In focal group (n=12), the mean total macular volume was 7.63 cubic mm prior to laser photocoagulation and 7.52 cubic mm and 7.14 cubic mm, 1 and 3 months after laser therapy. This corresponds to decrease by 1.4% and 3.4% respectively.

In patients who underwent grid laser photocoagulation, mean total macular volume at baseline was 9.56 cubic mm and following laser therapy decreased to 8.86 cubic mm at 1 month and 8.49 cubic mm at 3 months, corresponding to decrease in mean total macular volume by 7.3% and 11.2% respectively.

There was a decrease in the total macular volume in all the groups. This, however, was present even when there was an increase in the retinal thickness both in central fovea and in the perifoveal region in focal group. Further studies with larger no of patients and longer duration of follow up can help in solving the disparity that existed in our study for which an association could not be established.

The aim of DME treatment should primarily be improvement or stabilization of VA and secondarily prevention of further vision loss. Therefore, new laser

treatment strategies should be developed to minimize chorioretinal damage in eyes with less severe retinal thickening at the center of the macula, while maintaining similar treatment efficacy.

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