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Original Research Article

Effect of pan retinal photocoagulation on macular ganglion cell - inner plexiform layer and peripapillary retinal nerve fibre layer thickness

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ABSTRACT

Purpose: To determine the effect of pan retinal photocoagulation (PRP) on spectral domain optical coherence tomography (SD OCT) morphologic parameters like macular ganglion cell-inner plexiform layer (GCIPL), peripapillary retinal nerve fibre layer (RNFL) thickness and central macular thickness (CMT) in diabetic retinopathy cases.

Materials and Methods: This is a retrospective study including 52 eyes with severe non-proliferative to proliferative diabetic retinopathy without macular oedema who required PRP. Macular GCIPL, CMT and peripapillary RNFL thickness measured at baseline and at 1-, 6-, 12- and 18-months post PRP with SD OCT.

Result: CMT, Macular GCIPL and peripapillary RNFL thickness increased significantly at 1 month ($p<0.05$), thereafter a decreasing trend noted at 6, 12 and 18 months. At 18 month CMT, GCIPL and RNFL thickness are higher than baseline but not statistically significant except temporal RNFL and Average GCIPL ($p<0.05$). A significant correlation found between changes in temporal RNFL and average GCIPL thickness (Pearson Correlation coefficient r= 0.652, 0.557, 0.782, 0.624 at 1, 6, 12 and 18 months respectively. $P<0.05$ for all values)

Conclusion: CMT, macular GCIPL and peripapillary RNFL thickness increase following PRP; peaking at month 1 and stabilizing through next 18 months. Macular GCIPL thickness could be a reproducible indicator of temporal RNFL.

1. Introduction

Pan retinal photocoagulation (PRP) is the standard treatment in severe non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) without clinically significant macular edema (CSME). The efficacy has been clearly demonstrated by Diabetic Retinopathy Study and Early Treatment Diabetic Retinopathy Study.[1–3] PRP can have adverse effects like macular edema, loss of foveal contrast sensitivity, field defects, epiretinal membranes as shown by various studies.[4–6] To quantify the structural changes after PRP in diabetic retinopathy cases that could possibly affect visual function, various studies have been done considering parameters like Retinal Nerve Fibre Layer (RNFL) thickness, macular thickness.[7–9] With improved segmentation algorithms in modern Spectral Domain Optical Coherence Tomography (SD OCT), macular ganglion cell layer-Inner Plexiform Layer thickness

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(GCIPL) thickness has become an important parameter, has been evaluated in glaucoma,[10,11] multiple sclerosis[12,13] and found to have same diagnostic performance as RNFL. In diabetic retinopathy, very few studies have been done to evaluate long term changes in ganglion cell layer after PRP.[14]

Our primary objective is to compare the changes in quantitative macular parameters pre- and post PRP laser in severe NPDR and PDR cases without CSME. Our secondary objective is to find out if there is any correlation between RNFL and GCIPL exists.

2. Materials and Methods

This is a retrospective data analysis of all patients with type 2 diabetes mellitus having severe NPDR or PDR, without macular edema who underwent PRP laser between July 2014 to July 2016 at our institute. Institutional Ethics Committee approval was obtained. In subjects where both eyes met the inclusion criteria, the eye with better vision was included for analysis. Detailed demographic, clinical characteristics, medical and ocular history were noted. Best corrected visual acuity (BCVA), intraocular pressure (IOP), slit-lamp examination findings of anterior segment and grading of diabetic retinopathy were done. Dilated fundus examination findings were compared with baseline fundus photograph and fundus fluorescein angiography (FFA) to out any discrepancy.

Patients with incomplete data, glycosylated haemoglobin level (HbA1c) ≥ 8%, any intravitreal injection in the study eye within 4 months before PRP, high risk PDR cases, patients requiring vitrectomy or other surgical intervention within 18 months follow up period, poor quality OCT images were excluded from study.

2.1. OCT images

OCT images of CIRRUS HD-OCT MODEL 500 (Carl Zeiss Meditec Jena,Germany) were used. Well centred scans with signal strength of ≥ 7 were selected. Optic Disc Cube 200×200 protocol used to obtain average and four quadrant (superior, inferior, nasal, temporal) RNFL thickness. Macular Cube 200×200 protocol used which consists of three concentric circles of a central circle and inner and outer rings with diameters of 1, 3 and 6 mm, respectively. CMT was defined as the thickness of central circle with 1 mm diameter (Central Subfield Thickness). Average GCL+ IPL (GCIPL) thickness along with six sectoral thickness values, from each of the six 60˚ segments: superotemporal, superior, superonasal, inferonasal, inferior and inferotemporal obtained. The GCA algorithm 6.0 software version used for data processing which detects and measures the macular GCIPL thickness within a 14.13 mm^2 elliptical annulus area centred on the fovea with an vertical inner and outer minor axis radius of 0.5 mm and 2.0 mm respectively and horizontal inner and outer major axis radius of 0.6 mm and 2.4 mm, respectively.

2.2. Pan retinal photocoagulation

PRP was done using 514 nm argon green laser (Carl Zeiss Meditec AG 07740, Jena, Germany). A single surgeon completed PRP in 4 sittings over 2 weeks. Area of laser extended one disc diameter beyond vascular arcades and optic nerve head to beyond equator. Laser pulse duration and spot size were 100 ms and 300 μ respectively and were placed at one burn-width apart. The total number of burns was approximately 2000.

Follow up data from month 1, 6, 12 and 18 after PRP were collected and analysed.

2.3. Statistical analysis

Statistical package for social sciences (SPSS-22) have been used to analyse the data. For continuous data normality was tested using KS test. To compare the mean score in repeated observations, repeated-measures ANOVA have been used. Paired sample t- test was used to compare the mean difference between the groups. Pearson correlation coefficient was used to test the linear relationship between the groups. For all calculation, P value < 0.05 has been considered statistically significant. For analysis, BCVA was converted to the logarithm of the minimum angle of resolution (log MAR).

3. Results

Fifty two eyes of 52 subjects included for analysis. All demographic and clinical characteristics are shown in Table 1.

Table 1: Demographic and clinical profile

Demographic and Clinical Parameters	Values (Mean±SD)
Number of eyes (n)	52
Age (years)	52.7±8.2
Gender: M/F (n)	35/17
Duration of DM (years)	13.0±5.1
HbA1c (%)	6.7±1.5
Systemic HTN (n)	28
BCVA (log MAR Snellen)	0.09±0.10
IOP (mm Hg)	15.1±3.4
State of diabetic retinopathy (n) Severe NPDR / Non-high-risk PDR	19/33

DM- Diabetes mellitus; HbA1c- Glycosylated haemoglobin; HTN- Hypertension; BCVA- Best corrected visual acuity; log MAR- logarithm of minimum angle of resolution; IOP- Intraocular pressure; NPDR- Non proliferative diabetic retinopathy; PDR- Proliferative diabetic retinopathy

Changes in CMT: At one month post PRP, the mean CMT increased significantly from baseline (p<0.05). Thereafter, a decreasing trend was observed at 6,12 and

Table 2: Mean score change in parameters over the time

Parameters	Time in Months					
	Baseline	1 month	6 months	12 months	18 months	**P value***
Average CMT (μm)	272.33 ±13.05	274.98 ±13.62	274.19 ±14.54	274.12 ±13.11	273.46 ±12.27	<0.001
Average RNFL Thickness (μm)	92.33 ± 15.75	96.77 ± 15.76	95.77 ± 14.29	95.35 ± 13.98	94.54 ± 15.03	<0.001
Average GCIPL thickness (μm)	81.94±7.15	83.48±6.59	83.08±5.96	82.94±6.26	82.81±6.54	<0.001

Data are presented in Mean ± Standard deviation CMT- Central macular thickness, RNFL- Retinal nerve fibre layer Thickness, GCIPL- Ganglion Cell Inner Plexiform Layer

***Repeated Measures ANOVA test used**

Paired samples t test use, p value < 0.05 significant : Average CMT (baseline & 1 month), Average RNFL (baseline & 1 month), Average GCIPL (baseline & 1 month, Baseline & 18 months)

18 months but value was not significant as compared to 1 month value. At 18 months follow up mean CMT was higher than that of baseline but was not statistically significant.

Changes in peripapillary RNFL: The changes in average, superior, inferior, nasal and temporal quadrant RNFL thickness were same with a significant post PRP increase in thickness at 1 month from baseline (p<0.05), thereafter decreased at 6,12 and 18 months. Neither these values were clinically significant when compared to one month value nor the baseline.

Changes in Macular GCIPL: The macular GCIPL thickness (average and all sectors) increased significantly at 1 month from baseline (p<0.05) and then decreased in a same pattern as CMT and RNFL.

The mean score changes in all the parameters over time is shown in Table 2.

A significant correlation was seen between temporal RNFL and average GCIPL thickness (Pearson Correlation coefficient r= 0.652, 0.557, 0.782, 0.624 at 1, 6, 12 and 18 months respectively. P<0.05 for all values). (Figure 1)

The mean baseline BCVA (Snellen log MAR) was 0.09±0.10. No significant change in visual acuity was noted at each follow up in comparison to baseline visual acuity (P>0.05).

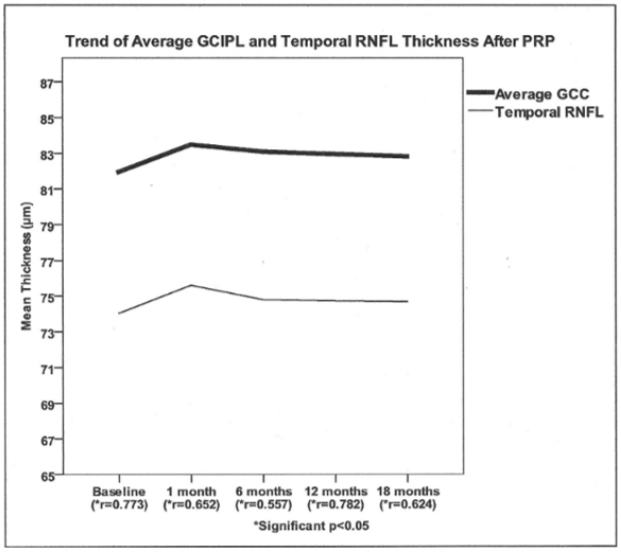

Figure 1: Linear relationship between changes in Average Macular Ganglion Cell Inner Plexiform Layer (GCIPL) thickness and Temporal Retinal Nerve Fibre Layer (RNFL) Thickness after PRP over 18 months. Pearson Correlation Coefficient was significant (P<0.05) between the two groups at baseline, 1,6,12,18 months

4. Discussion

In our study CMT, Macular GCIPL and peripapillary RNFL thickness increased significantly at 1 month (p<0.05), thereafter a decreasing trend noted at 6,12 and 18 months. At 18 months CMT, GCIPL and RNFL thickness are higher than baseline but not statistically significant except temporal RNFL and Average GCIPL (p<0.05). The thickenings of different layers of retina could be explained by PRP-induced retinal inflammation and oedema in the early post-PRP phase. Nonaka et al[15] reported that PRP augmented retinal vascular permeability due to the accumulation of leukocytes in untreated area also. Other studies have shown up regulation of vascular endothelial growth factor (VEGF) after photocoagulation[16] and VEGF induced increased retinal vascular permeability.[17,18] Temporal RNFL formed by macular ganglion cells suggests a possible relationship in their changes.

The initial thickening of CMT and RNFL at 1 month post PRP was comparable to other studies but after 1 month the pattern of CMT and RNFL changes differed.[7–10] Very few reports obtained for comparison of macular ganglion cell layer changes. We noted a significant correlation between average GCIPL and temporal RNFL thickness at each follow up which was similar to findings of Kim JJ et al[14] but the pattern of GCIPL and RNFL changes is different in both studies. Although both studies used same CIRRUS HD-OCT machine with high reproducibility still a larger sample size is perhaps required to explain the inconsistency in results.

The strength in our study remained in that we assessed three parameters macular GCIPL, CMT and RNFL simultaneously to quantify changes in them after PRP and to find any correlation if exist between them; observation period was longer than previous similar study; good glycemic control maintained throughout follow up period.

Still, there are some limitations of our study. We evaluated only visual acuity change after PRP but neglected other functional aspects like contrast sensitivity. Also, we did not correlate visual acuity to individual parameter.

5. Conclusion

Macular GCIPL thickness by spectral domain OCT could be an appropriate reproducible indicator of the temporal RNFL and can be used as a supplementary tool in diagnosing early cases of RNFL damage. Further, studies considering other functional aspects would be necessary to evaluate the mechanism and clinical implications of GCIPL thickening after PRP.

6. Source of Funding

None.

7. Conflict of Interest

None.

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