

CHANGES IN RETINAL NERVE FIBER LAYER ON OPTICAL COHERENCE TOMOGRAPHY AFTER PANRETINAL PHOTOCOAGULATION IN PATIENTS WITH PROLIFERATIVE DIABETIC RETINOPATHY

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ABSTRACT

OBJECTIVE: To study changes in retinal nerve fiber layer (RNFL) measured on optical coherence tomography (OCT) after panretinal photocoagulation (PRP) in patients with proliferative diabetic retinopathy (PDR).

METHODS: This quasi experimental study was conducted at Department of Ophthalmology, Lahore General Hospital, Lahore from 1-4-2017 to 30-3-2018. All patients (n=38) diagnosed with PDR requiring PRP were included. Patients having any coexisting ocular pathology hindering the OCT measurement were excluded. Pre-operatively, RNFL thickness in four quadrants and signal strength was measured on OCT and visual acuity (VA) on Snellen's chart. Post-operatively, patients were followed-up after one-month and three-months and VA was measured and OCT performed.

RESULTS: The mean age of patients was 60.66 ± 5.51 years with 23(60.5%) males. PRP was performed in right-eye of 22 patients. Pre-laser VA in 28 patients was 6/60. Pre-laser total RNFL was $84.32 \pm 4.78 \mu\text{m}$ reduced to $83.74 \pm 4.61 \mu\text{m}$ one-month and $81.89 \pm 4.40 \mu\text{m}$ three-months post-laser ($p < 0.001$). Pre-laser, superior RNFL thickness was $84.97 \pm 4.13 \mu\text{m}$, reduced to $84.39 \pm 3.95 \mu\text{m}$ one-month and to $82.21 \pm 3.84 \mu\text{m}$ at three-months post-laser ($p = 0.024$). Pre-laser inferior RNFL thickness was $84.89 \pm 4.68 \mu\text{m}$, reduced to $84.00 \pm 4.44 \mu\text{m}$ one-month and to $81.71 \pm 4.50 \mu\text{m}$ three months post-laser ($p = 0.032$). Pre-laser temporal RNFL thickness was $83.26 \pm 3.47 \mu\text{m}$, reduced to $82.34 \pm 3.44 \mu\text{m}$ one-month and to $80.21 \pm 3.49 \mu\text{m}$ three-months post-laser ($p < 0.001$). Pre-laser nasal RNFL thickness was $85.16 \pm 3.78 \mu\text{m}$, reduced to $84.26 \pm 3.88 \mu\text{m}$ one-month post-laser and to $82.08 \pm 3.74 \mu\text{m}$ at three-months post-laser ($p = 0.043$). Pre-laser, signal strength on OCT was 8.26 ± 0.69 and 8.66 ± 0.48 after one-month post-laser and 8.55 ± 0.50 at three-months laser ($p = 0.009$).

CONCLUSION: PRP leads to a decrease in thickness of RNFL after one month and three months as compared to pre-laser RNFL thickness.

KEY WORDS: Retina (MeSH); Panretinal photocoagulation (Non-MeSH); Retinal nerve fiber layer thickness (Non-MeSH); Diabetic Retinopathy (MeSH); Tomography, Optical Coherence (MeSH); Neovascularization, Pathologic (MeSH); Laser Coagulation (MeSH).

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INTRODUCTION

Diabetes mellitus is one of the leading metabolic diseases around the globe. Like other systems, it also affects

the eye. The most common ocular involvement of diabetes mellitus is involvement of the retinal blood vessels called diabetic retinopathy.¹ Diabetic retinopathy is thought to be one of the

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leading causes of visual impairment around the world.^{2,3} Proliferative diabetic retinopathy is an advanced stage of diabetic retinopathy which occurs due to poor long term glycemic control and is more prevalent in type 1 diabetics as compared to type 2 diabetics.⁴ Proliferative diabetic retinopathy involves the development of neovessels which can bleed and lead exudative materials leading to macular edema and vitreous hemorrhage or tractional retinal detachment in advanced cases.⁵ Diabetic retinopathy is affected by many systemic factors such as hypertension, nephropathy, glycemic control and history of cigarette smoking.^{6,7}

Panretinal photocoagulation is the standard treatment for the treatment of proliferative diabetic retinopathy. In panretinal photocoagulation, peripheral retina is ablated with Argon laser in order to convert the ischemic retina into dead retina.⁸ Thus the resulting dead retina does not produce vascular endothelial growth factor which is mainly responsible for the formation of neovessels in proliferative diabetic retinopathy. Various modalities are available for the panretinal photocoagulation i.e. conventional Pan Retinal Photocoagulation (PRP), Pattern Scanning Laser (PASCAL) and Non-Microscopic Imaging Laser (NAVILAS).^{9,10}

Retinal nerve fiber layer is a vital layer of retina which is affected by many ocular diseases as well as ocular intervention.¹¹ Optical coherence tomography is a non-invasive retinal imaging tool which acquires three dimensional images of retina and helps in the layer by layer analysis of retina.¹² Various models of optical coherence tomography are available which measure retinal nerve fiber layer thickness and helps in understanding the ultra-structural changes in this vital layer.¹³ Lack of local literature on this issue was the rationale

TABLE I: CHANGES IN VISUAL ACUITY OF THE STUDY SUBJECTS BEFORE AND AFTER PANRETINAL PHOTOCOAGULATION

Visual Acuity	Pre-PRP	3 Months Post-PRP	P value
6/36	10 (26.3%)	12 (31.6%)	
6/60	28 (73.7%)	26 (68.4%)	0.804

PRP=panretinal photocoagulation; P-value was calculated by McNemer's Test.

to conduct this study.

METHODS

Ethical approval for this quasi experimental study was obtained from the ethical review committee of Lahore General Hospital, Lahore. Patients who were known diabetics and having poor long term glycemic control presenting to Ophthalmology Out Patient Department, Lahore General Hospital from 1st April, 2017 to 30th March, 2018 were assessed for inclusion and exclusion criteria. Patients (n=38)¹⁵ diagnosed with proliferative diabetic retinopathy on slit lamp fundus examination, requiring panretinal photocoagulation were selected by non-probability consecutive sampling and were included in study. Patients diagnosed with any co-existing ocular disease such as retinal detachment, vitreous hemorrhage, visually significant cataract hindering optical coherence tomography (OCT) measurement and corneal or any other media opacity were excluded from study.

Patients were counselled about the stage of diabetic retinopathy and negative impact on vision if not treated. Informed consent was obtained from all

patients before performing laser. Pre-laser age, gender and laterality was recorded on proforma. Retinal nerve fiber layer thickness was measured along with signal strength (quantification of the OCT waves to penetrate certain tissue) on OCT and documented on the proforma. After aseptic measure, pupils were pharmacologically dilated in the eye to be lased.

Patients were then seated on the slit lamp laser delivery system and laser was applied. Post-laser patients were prescribed antibiotic eye drops four times daily for one week and non-steroidal anti-inflammatory drug (NSAID) tablet three times daily for one week. Patients were called for followup after one and three months at which time OCT was again performed to measure and document the thickness of retinal nerve fiber layer and signal strength.

Data was entered and analyzed using statistical package for social sciences (SPSS) software version 22. Frequencies and percentages were calculated for categorical variables while mean and standard deviation were calculated for numerical variables. Visual acuity between pre-PRP and

post-PRP was assessed by McNemer's test. The difference between pre-laser and post-laser treatment (pre-laser, 1 month post-laser and 3 month post-laser) was determined by repeated measures ANOVA test and further assessment was checked by Bonferroni Test. Statistical significance was defined as p-value of =0.05 with 95% confidence interval.

RESULTS

The mean age of patients was 60.66±5.51 years. There were 23 (60.5%) males and 15 females (39.5%) included in the study. Panretinal photocoagulation was performed in right eye of 22 (57.9%) patients and 16 (42.1%) left eyes of patients. Visual acuity in 28 (73.7%) patients was 6/60 pre-laser while the other 10 (26.3%) had a pre-laser visual acuity of 6/36. After three months post-laser, 26 (68.4%) patients had a visual acuity of 6/60 while the remaining 12 (31.6%) patients had a visual acuity of 6/36 as measured on Snellen's chart (Table I).

Mean pre-laser, total retinal nerve fiber layer thickness was 84.32±4.78µm which reduced to 83.74±4.61µm after one month and 81.89±4.40µm at three months after laser (p<0.001). Mean post-laser retinal nerve fiber layer thickness decreased significantly in all the four quadrants after one and three months of panretinal photocoagulation as compared to pre-laser retinal nerve fiber layer thickness (Table II).

TABLE II: CHANGES IN RETINAL NERVE FIBER LAYER THICKNESS BEFORE AND AFTER PANRETINAL PHOTOCOAGULATION (n=38)

Parameter	Pre-PRP	1 Month Post-PRP	3 Month Post-PRP	P* value	P** value	P*** value	P**** value
Total Retinal Nerve Fiber (µm)	84.32±4.78	83.74±4.61	81.89±4.40	<0.001	0.034	0.023	0.043
Superior Retinal Nerve Fiber (µm)	84.97±4.13	84.39±3.95	82.21±3.84	0.024	0.008	0.001	0.023
Inferior Retinal Nerve Fiber (µm)	84.89±4.68	84.00±4.44	81.71±4.50	0.032	0.033	<0.001	0.022
Temporal Retinal Nerve Fiber (µm)	83.26±3.47	82.34±3.44	80.21±3.49	<0.001	0.012	0.032	<0.001
Nasal Retinal Nerve Fiber (µm)	85.16±3.78	84.26±3.88	82.08±3.74	0.043	<0.001	0.021	0.013
Signal Strength	8.26 ± 0.69	8.66 ± 0.48	8.55±0.50	0.009	0.003	0.163	0.999

PRP=panretinal photocoagulation; Continuous variables were presented as Mean±Standard Deviation; P*=Repeated measures ANOVA was applied; Bonferroni Post Hoc Test: P** (Pre-PRP versus Post-PRP 1 month), P*** (Pre-PRP versus Post-PRP 3 month), P**** (Post-PRP 1 month versus Post-PRP 3 month).

DISCUSSION

The authors present the changes in retinal nerve fiber layer thickness after panretinal photocoagulation for the treatment for proliferative diabetic retinopathy. In this study, retinal nerve fiber layer thickness decreased significantly in all the four quadrants as well as in global thickness after one and three months of panretinal photocoagulation. The signal strength also changed on OCT after one and three months of panretinal photocoagulation but it was not statistically significant.

Kim and Cho have studied the changes in parapapillary retinal nerve fiber layer thickness after panretinal photocoagulation for diabetic retinopathy. They documented a decrease of 2.12 microns after six months of panretinal photocoagulation which was not statistically significant.¹⁴ Lim MC and associates compared the retinal nerve fiber layer thickness between normal eyes, diabetic eyes which undergo panretinal photocoagulation and diabetic eyes that did not undergo panretinal photocoagulation. They found a statistically significant differences in retinal nerve fiber layer thickness in inferior and nasal quadrants between the three groups. The temporal retinal nerve fiber layer thickness was comparable among groups.¹⁵

Lee SB, et al. have studied the longitudinal changes in retinal nerve fiber layer thickness after pan retinal photocoagulation. Their study showed an increase in the mean and all quadrants retinal nerve fiber layer thickness at six months, after six months of panretinal photocoagulation only to be decreased later on at twenty four months post panretinal photocoagulation. Both the increase and then decrease in the thickness of retinal nerve fiber layer was statistically significant.¹⁶

Kim J and colleagues have studied the temporal changes in parapapillary retinal nerve fiber layer thickness before and after panretinal photocoagulation. Their study depicted an increase in average retinal nerve fiber layer thickness at three months after

panretinal photocoagulation which later on decreased 108.4 microns to 103.5 microns at twenty four months. Based on these findings they concluded that the retinal nerve fiber layer undergoes thickening after panretinal photocoagulation for three months which subsequently if followed by significant thinning at two years.¹⁷

Muqit MM and associates have studied the effects of argon panretinal laser photocoagulation on retinal nerve fiber layer. This study showed an increase in mean retinal nerve fiber layer thickness by 8 microns at ten weeks as compared to baseline and then it decreased by 3.99 microns at six months as compared to baseline.¹⁸

Muqit MM, et al. conducted a randomized trial on the effects of single session panretinal photocoagulation versus multiple session (over 4 weeks) panretinal photocoagulation delivered by PASCAL system. The single session group showed non-significant increase of total retinal nerve fiber layer thickness by 7.2 microns at four weeks which then decreased by 1.2 microns from baseline at twelve weeks. However, the multisession group showed a statistically significant increase of total retinal nerve fiber layer thickness by 3.1 ± 5.4 microns at four weeks which later on decreased by 3.5 ± 6.3 microns from baseline at twelve weeks.¹⁹

Park YR and associates have compared the changes in retinal nerve fiber layer after conventional versus PASCAL pan retinal photocoagulation. The conventional laser group showed a significant decrease in retinal nerve fiber layer thickness (3.70 ± 4.24 microns, $p < 0.001$) while the PASCAL laser group did not show significant changes in retinal nerve fiber layer thickness from baseline at six months after panretinal photocoagulation. After one year of laser, the PASCAL group did not show any significant change in retinal nerve fiber layer thickness while the conventional group again showed significant reduction in thickness of retinal nerve fiber layer (5.42 ± 3.69 microns, $p < 0.001$).²⁰

Lee DE, et al. have studied the effects of

Pattern Scan laser photocoagulation on parapapillary retinal nerve fiber layer thickness. The average retinal nerve fiber layer thickness increased by 0.84 microns (99.11 ± 18.91 microns) at two months post-laser and decreased by 0.4 microns (97.87 ± 18.79 microns) at six months as compared to baseline (98.27 ± 18.97 microns). All the changes were statistically insignificant.²¹

Shin HJ and colleagues have studied the effects of multiple intravitreal injections for various retinal diseases on retinal nerve fiber layer. They enrolled the patients with diabetic macular edema (DME), age related macular degeneration (AMD) and retinal vein occlusion (RVO) who had received at least three intravitreal anti-VEGF injections. The retinal nerve fiber layer thickness did not change in the AMD group while it decreased from 100 microns to 97.1 microns in DME group and from 101.8 microns to 98.0 microns in RVO group. However, the number of injections had no correlation with the changes in retinal nerve fiber layer.²²

Hwang DJ, et al. have compared the retinal nerve fiber layer profiles between eyes with and without diabetic macular edema (DME). They found an increased global retinal nerve fiber layer thickness in patients with diabetic macular edema as compared to those without it. The retinal nerve fiber layer thickness correlated with the central macular thickness and decreased in response to anti-VEGF injections treatment as the central macular thickness was reduced subsequently.²³

CONCLUSION

Retinal nerve fiber layer thickness decreases after one and three months of panretinal photocoagulation.

LIMITATION AND RECOMMENDATION

The followup period in this study was three months. The authors recommend large randomized controlled trials with longer followup period to better understand the effects of panretinal photocoagulation on the anatomy of retina.

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AUTHORS' CONTRIBUTIONS

Following authors have made substantial contributions to the manuscript as under:

MS: Concept & study design, acquisition of data, drafting the manuscript, critical review, final approval of the version to be published.

AA: Acquisition of data, drafting the manuscript, final approval of the version to be published.

AR: Acquisition, analysis & interpretation of data, drafting the manuscript, final approval of the version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest

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