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Assessment of Effects of Pan-Retinal Photocoagulation on Retinal Nerve Fibre Layer By Optical Coherence Tomography

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ABSTRACT

Objective: To assess the Retinal Nerve Fiber Layer by Optical Coherence Tomography in patients treated with pan-retinal photocoagulation at one-month and three-month post-treatment follow-up.
Study Design: Prospective longitudinal study.
Place and Duration of Study: Combined Military Hospital, Quetta Pakistan, from Oct 2022 to Apr 2023.
Methodology: A total of 77 Patients with 104 diseased eyes were included in the study. Forty-eight patients were male, while 29 were female. Out of 77 patients, 63 patients were diagnosed with Proliferative Diabetic Retinopathy, out of which 27 patients had Proliferative Diabetic Retinopathy in both eyes (54 eyes) and 36 had DR in one eye (36 eyes). Six patients were diagnosed cases of central retinal vein occlusion (6 eyes), four patients had Eales disease (8 eyes), and three patients had uveitis (3 eyes). Retinal Nerve Fiber Layer was assessed by Optical coherence tomography in patients before performing pan-retinal photocoagulation and at follow-up visits at one- and three-months post- pan-retinal photocoagulation.
Results: Before pan-retinal photocoagulation, the average thickness of the Retinal Nerve Fiber Layer in the corresponding geographical area was 84.18±2.62 µm. However, there was a decrease, with the thickness being observed to be 83.46±3.75 µm one month after pan-retinal photocoagulation and further dropping to 81.55±2.58 µm three months after pan-retinal photocoagulation. This indicates a regression in the disease progression.
Conclusion: Regular follow-up of our patients indicates significant changes in Retinal Nerve Fiber Layer thickness when assessed at one month and three months post-PRP.PRP is a promising treatment modality in patients suffering from retinal diseases.

Keywords: Eales diseases, Optical coherence tomography, Proliferative diabetic retinopathy, Proliferative diabetic retinopathy, Pan-retinal photocoagulation, uveitis.

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INTRODUCTION

Pan-retinal photocoagulation (PRP) has been described as the standard treatment for conditions affecting the retina. It has proven to considerably lessen the risk of developing morbid complications such as visual loss.[1] Guidelines from the American Academy of Ophthalmology, as well as the Royal College of Ophthalmologists, have recommended PRP as a first-line treatment modality for proliferative diseases.[2] PRP employs laser technology to focus on the retina, converting an ischemic retina into a non-functioning one. This reduces its need for oxygen and metabolic support, preventing the progression of proliferative changes. It achieves this by utilizing a double-frequency NdYAG laser.[3] Despite the multiple proven benefits and outcomes of PRP, it is known to cause several side effects, including changes such as photoreceptor loss, retinal pigment epithelium changes, and thermal damage due to high temperatures involving the whole retinal cell layer.[4] Studies have observed that PRP can also induce thinning of the retinal nerve fiber layer (RNFL) in treated patients. These patients have been regularly followed up for up to 2 years post-PRP.[5,6]

Amongst the many imaging modalities available to evaluate RNFL, Optical coherence tomography (OCT) is frequently used. OCT is a newly developed, safe, rapid, and non-invasive technique that can help treating ophthalmologists take in-depth customized retina scans.[7,8] Multiple repeated scans can be done at the exact location in the retina, and detailed structural images are taken of the RNFL and retinal vasculature.[9,10]

Our study aims to ascertain the effects and changes incurred by pan-retinal photocoagulation (PRP) on the retinal nerve fiber layer (RNFL) affected by different retinal conditions, such as proliferative

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diabetic retinopathy (PDR), central retinal vein occlusion (CRVO), Eales disease, and uveitis. These effects will be assessed by OCT, and their outcome will be observed through regular follow-ups with the treated patients.

METHODOLOGY

The prospective longitudinal study was conducted at Combined Military Hospital, Quetta Pakistan, from January to December 2022 after obtaining approval from the Institutional Review Board (vide reference number CMH QTA/IRB/040 dated 23/Aug 2023). We calculated a sample size via the WHO calculator, keeping the prevalence of diabetic retinopathy of 7.3%.[11] Sampling was done using a non-probability consecutive sampling technique.

Inclusion Criteria: The study included patients diagnosed with different ophthalmic conditions affecting the retina, such as proliferative diabetic retinopathy (PDR), central retinal vein occlusion (CRVO), Eales disease, and uveitis. All of these patients were treated with PRP as the sole treatment modality. None of these patients had received any previous PRP treatment, i.e., treatment-naive.

Exclusion Criteria: The study excluded patients with concurrent ocular conditions like retinal detachment, bleeding in the vitreous, significant vision-affecting cataract, or corneal opacity. It also excluded patients with glaucoma or any other causes of optic atrophy that might lead to ganglion cell loss.

Patients were informed about the complete details of their disease stage. They were also informed about the impact the disease might have on their vision if they were not treated in a timely manner. Consent was obtained from all patients before the procedure. Before laser treatment, the thickness of the retinal nerve fiber layer was assessed, and the signal strength was recorded using the RS 3000 OCT device by Nidek. These measurements were documented in the patient information record.[12,13] After implementing sterile precautions, the eye to be treated was dilated using Tropicamide or Mydriacyl eye drops. A contact lens was placed on the slit lamp laser delivery system, and a double-frequency NdYAG laser was utilized. A total of 2000-2500 burns were administered, with a spot size of 200 microns, pulse duration of 100 milliseconds, and a power of 250-300 milliwatts. Following the procedure, patients were instructed to use Tobradex antibiotic eye drops four times daily for one week and to take NSAID tablets three times daily for the same duration. Patients were advised to schedule a follow-up visit with the Ophthalmology Department after one and three months post pan-retinal photocoagulation, during which another OCT examination would be conducted to measure and record the retinal nerve fiber layer thickness.[13]

Data was analyzed using Statistical Package for Social Sciences, SPSS version 26. Baseline variables were analyzed descriptively using frequencies and percentages for qualitative variables and mean with standard deviation for continuous variables. A statistically significant difference was noticed in RNFL thickness before and after intervention (One month and three months post-PRP). It was assessed using repeated measures of the ANOVA Test. The *p*-value of ≤ 0.05 was taken as significant.

RESULTS

A total of 77 Patients with 104 diseased eyes were included in the study. Of the patients, 48(62.3%) were male and 29(37.7%) were female. The mean age was 57.48±4.77 years, ranging from 32 to 72.

Out of 77 patients, 63 patients were diagnosed with ProliferativeDiabetic Retinopathy, out of which 27 patients had DR in both eyes (54 eyes) and 36 had DR in one eye (36 eyes). Six patients were diagnosed cases of CRVO (6 eyes), four patients had Eales disease (8 eyes), and three patients had uveitis (3 eyes). The distribution of the patients and eyes is shown in Table-I.

Table-I: Distribution of Patients with Diseased Eyes (n=77)

Disease	Patients (n=77)	Eyes (n=104)
Proliferative Diabetic Retinopathy	63(81.8%)	90(86.5%)
Central retinal vein occlusion	6(7.8%)	6(5.8%)
Eales	4(5.2%)	4(3.8%)
Uveitis	4(5.2%)	4(3.8%)

Table-II displays the variations in RNFL thickness according to the study parameters. Before photocoagulation treatment (Pre-PRP), the average geographical RNFL thickness was 84.18±2.62 µm. This value decreased to 83.46±3.75 µm one month after PRP and further declined to 81.55±2.58 µm three months after PRP. The average pre-PRP Superior RNFL thickness was 84.22±3.42 µm, which reduced to 82.44±3.38 µm after one month of PRP and reached 80.21±2.23 µm after three months of PRP. Additionally, the mean inferior RNFL thickness before PRP was 83.09±3.10 µm, decreased to 82.94±2.99 µm one month post-PRP, and ultimately measured 80.16±2.05 µm at three months after PRP. Before PRP, the average thickness of the superonasal RNFL was 84.87±4.13 µm. Following PRP treatment, it decreased to 83.03±2.87 µm after one month and further dropped to 81.11±2.90 µm at three months post-PRP. Regarding the supero-temporal RNFL, its mean thickness before PRP was 83.47±2.25 µm. After one month of PRP, it reduced to 82.55±2.15 µm, and at three months post-PRP, it further decreased to 80.61±2.10 µm. Before performing pan-retinal photocoagulation (PRP), the average thickness of the inferonasal retinal nerve fiber layer (RNFL) was 83.13±2.33 µm. After one month of PRP, this thickness decreased to 81.32±2.19 µm, and after three months, it further reduced to 79.45±2.29 µm. Similarly, the average thickness of the inferotemporal RNFL pre-PRP was 81.13±2.13 µm, which decreased to 80.26 ± 1.95 µm after one month of PRP and further reduced to 79.32±1.89 µm at three months after PRP. The reduction in RNFL thickness after PRP was statistically significant (with a p-value < 0.05). The signal strength on optical coherence tomography (OCT) before PRP was 8.19±0.55 µm, which increased to 8.56±0.59 µm after one month of PRP and then slightly decreased to 8.35±0.49 µm after three months of PRP (p=0.009). A comparison of the changes in RNFL thickness between the groups is presented in Table-III.

observed a considerable decrease in the thickness of RNFL geographically and in all the six quadrants after the procedure. The signal strength on OCT was also observed to have changed after one- and three-month follow-up visits post-PRP. An important observation to note here is that these results do not show regression in the disease process directly but more so as a side effect of PRP, which eventually may result in visual field loss and decreased glare. Our patients were counseled in detail about these side effects before the procedure. As further discussed, we found multiple studies assessing the impact of treatments such as PRP on the thickness of RNFL. However, there needs to be more local studies and data which also served as the primary rationale for conducting this study and assessing the response in our local patient population.

A study by Mohamed *et al.* concluded that retinal nerve fiber layer (RNFL) thickness changed six months after laser treatment in patients suffering from PDR, with statistically significant differences before and after treatment.[14] A similar outcome was observed in a study by Huang *et al.* on 45 eyes with PDR in China. The study confirmed that PRP effectively decreased retinal ischemia and cushioned the retinal neurons. They also concluded that PRP effectively reverses diabetic microvascular, neural, and choroidal damage when patients were reassessed 12 months post-treatment visit.[15] In a meta-analysis presented by Wadhwani *et al.,* in which a total of 10 studies were

Table-II: Changes in RNFL Thickness (n=104)

Parameters	Pre-PRP (µm)	One Month's PRP (µm)	Three Months PRP (µm)	*p*-value
Total	84.18±2.62	83.46±3.75	81.55±2.58	0.001
Superior	84.22±3.42	82.44±3.88	80.21±2.23	0.001
Inferior	83.09±3.10	82.94±2.99	80.16±2.05	0.001
Supero-Nasal	84.87±4.13	83.03±2.87	81.11±2.90	0.001
Supero-Temporal	83.47±2.25	82.55±2.15	80.61±2.10	0.001
Infero-Nasal	83.13±2.33	81.32±2.19	79.45±2.29	0.001
Infero-Temporal	81.13±2.13	80.26±1.95	79.32±1.89	0.001
Signal Strength	8.19±0.55	8.56±0.59	8.35±0.49	0.001

Table-III: Intergroup Comparison of Changes in RNFL Thickness (n=104)

Parameters	Pre-PRP Vs One-Month Post-PRP	Pre-PRP Vs Three-Month Post-PRP	One-month Post-PRP Vs Three-Month Post-PRP
Total	0.041	0.043	0.023
Superior	0.032	0.035	0.025
Inferior	0.034	0.031	0.001
Supero-Nasal	0.034	0.035	0.046
Supero-Temporal	0.034	0.011	0.012
Infero-Nasal	0.041	0.06	0.015
Infero-Temporal	0.042	0.002	0.01
Signal Strength	0.004	0.163	0.99

DISCUSSION

Our study presents the changes observed in RNFL thickness after PRP for treating conditions such as PDR, CRVO, Eales disease, and uveitis. Overall, we included with a total of 377 eyes of patients suffering from PDR, it was stated that various authors had reported a significant decrease in RNFL when they were assessed after two years post-PRP.[16] In another study by Kim *et al,* the average RNFL thickness (360 measurement) was reported to have been decreased markedly from 108.4 µm to 103.5 µm at a follow-up of 2 years post-treatment. Although the average RNFL thickness was observed to have increased slightly during the first follow-up visit at three months post-PRP, it gradually decreased, showing a statistically significant decrease at the two-year follow-up visit.[17] We found a study that compared PRP with intra-vitreous ranibizumab in a total of 146 eyes from patients suffering from PDR by Jampol *et al.* The study concluded that an increased thinning was observed in RNFL after intra-vitreous ranibizumab compared to the RNFL of eyes treated with PRP. However, it was also specified that the greater thinning rate is attributable to a lower degree of edema rather than axonal loss.[18] A systematic review by Li *et al.* presented the outcomes and benefits of using PRP in patients suffering from CRVO. They reviewed 11 studies and concluded that a significant decrease in corneal sub-basal nerve plexus parameters and average peripapillary RNFL thickness was observed at a post-treatment follow-up visit.[19]

In a case report by Kh *et al.* of a patient suffering from Eales disease, the outcome of retinal laser photocoagulation used as a sole treatment modality exhibited marked improvement of clinical and functional indices. Notable improvements included better visual acuity, stabilization in the central retinal sensitivity value, improvement in the clarity of ocular media, a decrease in neovascularization as well as macular edema in the diseased eye, which was in the proliferative stage, and stabilization of the process in the eye which was observed to be in the ischemic stage of the disease.[20] In a retrospective study conducted by Obeid *et al,* PDR patients who were lost to follow-up (LTFU) after either receiving PRP or intra-vitreal anti-VEGF treatment were compared. Patients were assessed at return visit after being LTFU and 6- and 12-months post return visit. It was concluded that patients who received only intravitreal anti-VEGF did not demonstrate favorable anatomic and functional outcomes after being LTFU as compared to the patients who received PRP.[21]

Many studies worldwide document the short-term and long-term benefits of PRP on diabetic eyes only; in our study, we have studied the effects of PRP in a broader disease range. Many studies have also compared PRP and its outcomes with other available treatment modalities. However, local studies and patient data are seriously lacking, and we recommend record keeping and regular follow-up of patients in our healthcare setups to determine which therapy carries better outcomes regarding patient satisfaction and disease cure.

LIMITATIONS OF THE STUDY

Although this was a prospective study with regular follow-up till three months post-treatment, we do feel the need for a longer regular follow-up of the patients to document long-term good or bad effects of the treatment, if any, which could not be done in our study as most patients were lost to follow up.

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CONCLUSION

Our study records follow-ups of patients treated with PRP for various conditions such as PDR, CRVO, Eales disease, and uveitis. The treatment outcomes of our patient indicate significant changes in RNFL thickness when assessed at one-month and three-month post-PRP sessions. We recommend using PRP as a successful treatment modality with promising outcomes for patient health.

Conflic to Interest: None.

Authors' Contribution

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

BS & AH: Data acquisition, data analysis, critical review, approval of the final version to be published.

FK & WY: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

TAK & AQ: Conception, data acquisition, drafting the manuscript, approval of the final 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.

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