Changes in Central Macular thickness after pan-retinal photocoagulation (PRP) treatment in Proliferative diabetic retinopathy.

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ABSTRACT

Purpose: This study evaluated the effect of Pan retinal photocoagulation (PRP) on macular thickness and visual acuity in patients with Proliferative diabetic retinopathy (PDR).

Methodology: This clinical case series followed 35 subjects with PDR who underwent PRP. Ethical approval was obtained from the research committee of Pak International Medical College and Hospital, Peshawar. Subjects underwent a baseline assessment, including visual acuity, refraction, slit-lamp microscopy, fundoscopy, and intraocular pressure measurement. Optical coherence tomography (OCT) was performed pre- and post-PRP to measure central macular thickness (CMT). A total of 1500–2000 mild to moderate burns were applied. Data analysis was conducted using SPSS Version 27, and paired T-tests was used to assess differences in pre- and post-treatment CMT values.

Result: The study participants' ages ranged from 32 to 65 years, with a mean age of 48.68. The pre-treatment CMT ranged from 231.51 to 244.49 µm (mean: 238.00 µm), while post-treatment CMT ranged from 239.42 to 245.85 µm (mean: 239.42 µm). The mean change in CMT was 1.42 µm. Significant increases in CMT were observed in both age groups (≤50 years, p=0.001; ≥50 years, p=0.002) and gender (males, p=0.002; females, p=0.001) after one month. The mean number of laser burns applied was 2013.

Conclusion: After one month, PRP significantly increased macular thickness in patients with PDR. The findings suggest that PRP is effective in managing proliferative diabetic retinopathy by altering retinal thickness, potentially impacting visual acuity outcomes.

Keywords: Diabetes Mellitus (DM), Proliferative diabetic retinopathy (PDR), Pan-retinal photocoagulation (PRP), Optical Coherence Tomography (OCT), Centeral macular thickness (CMT).

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INTRODUCTION

Diabetes Mellitus (DM) can cause a wide range of pathologies. Its pathologies range from mild to severe. It can also cause early cataracts and index myopia, and also extend up to proliferative diabetic retinopathy or advanced diabetic eye diseases like vitreous hemorrhage and tractional retinal detachment. [1,2] The development of proliferative diabetic retinopathy depends upon the onset of diabetes and its long-term glycemic control. [2]

Proliferative diabetic retinopathy (PDR) may develop when the microangiopathic alteration occurs due to persistent hyperglycemia, which leads to endothelial and pericyte cell damage in capillaries, which in turn leads to microaneurysms and capillary dropout.[3,4] At least one quadrant of the retina must be ischemic for the development of PDR, and this capillary dropout becomes the source of retinal ischemia, which may cause an imbalance between the angiogenic and antiangiogenic vascular growth factors.[5] Other factors like damage to the endothelial cells, activation of certain enzymes, and the thickening of the basement membrane may also lead to PDR.[6]

Once the condition reaches the proliferative stage its treatment option includes a special type of laser, emitting 532 nm green light spectrum, and the procedure is called pan-retinal photocoagulation (PRP). This spectrum is used to thermally coagulate the ischemic retina and leads to decrease in the angiogenic stimulus. It aims to stop the progression of the newly formed abnormal blood vessels which were formed due to decreased blood supply (ischemia). The strength of the PRP was assessed clinically by observing the reduction of vitreous hemorrhage, retinal hemorrhage, improvement of vascularity, and the reduction of retinal venous caliber. However, it is also important to keep in mind that PRP can also damage certain retinal cells, like photoreceptor cells, bipolar cells, and ganglion cells which in turn lead to clinically pale optic disc after a couple of weeks. Instead of its side effects, the primary goal of the PRP is to restore the imbalance between the angiogenic and antiangiogenic factors. Decreasing the demand for oxygen in the retina leads to decrease in the production of pro-angiogenic factors that aim to inhibit the growth of abnormal blood vessels and help to promote the existing blood vessels.

In clinical evaluation, Optical Coherence Tomography (OCT) is a tool used to assess the efficacy of PRP. It is a non-contact and non-invasive retinal imaging technique that helps in the accurate measurement of retinal parameters such as central macular thickness (CMT), and macular edema, and together with other factors, the morphological subtypes of macular edema may be one of the important factors for variation in treatment response in patients with PDR. Its principle is based on interferometer techniques and picking a super quality picture with a spatial resolution of 7-9 micrometers.[7,8,9] This study aimed to evaluate the pre and post-macular thickness and visual acuity improvement after 1months of follow-up.

METHODOLOGY

It was a clinical case series follow-up study. A total of 35 subjects were included in this study, having proliferative diabetic retinopathy in one or both eyes and having no history of surgery or PRP. Before the start of the study, ethical approval was obtained from the ethical research committee of Pak International Medical College and Hospital Hayatabad Peshawar. The study was explained to each patient, and signed consent forms were obtained. The selected subjects went through visual Acuity, refraction, slit-lamp Microscopy, and fundoscopy with 90D, and intraocular pressure was recorded by an applanation tonometer for each individual. Before measuring retinal thickness, the eye was dilated for a minimum of 6 mm with drops of tropicamide 1%. After dilation, OCT (HEIDELBERG Engineering OCT Spectralis) was performed before and after Pan-Retinal photocoagulation (PRP). The difference was obtained by calculating the mean of pre and post-macular thickness in micrometers with 1500 to 2000 burns of mild to moderate intensity.

All the gathered data were analyzed by using SPSS Version 27. Frequency and percentages were calculated for categorical variables while mean, mode, minimum, and maximum were calculated for continuous variables. A paired T-test was applied to measure pre and post-differences.

RESULTS

Table 1 shows Age ranges from 32 to 65 years, with a mean of 48.68 years. Pre-CMT values vary between approximately 231.51 and 244.49, with a mean of 238.00, while post-CMT values range from about 239.42 to 245.85, with a mean of 239.42. Changes in CMT fall between approximately 1.36 and 1.48, with a mean change of 1.42. The number of burns ranges from around 1902 to 2123, with a mean of 2013. Table 2 shows that the Baseline CMT increased after one month in all groups: by 1.09 in those ≤50 years (p=0.001), and by 1.6 in those ≥50 years (p=0.002). Males experienced a 1.01 increase (p=0.002), while females had a 1.1 increase (p=0.001).

Table 1: Baseline Characteristics of the Subjects

	Minimum	Maximum	Mean(Std)
Age	32	65	48.68±16.52
Pre CMT	231.51	244.49	238.00±6.49
Post CMT	239.42	245.85	239.42±6.43
Changes in CMT	1.36	1.48	1.42±0.06
Number of Burns	1902	2123	2013±110.76

Table 2: Pre-PRP and Post-PRP Baseline characteristics by using Paired T test.

Variables	Baseline	After one month	Mean difference	Confidence Interval		P-value
				Lower	Upper	
≤50 years	239.01±6.72	240.10±6.78	1.09±0.06	0.0678	0.0987	0.001
≥50 years	238.27±7.65	239.87±7.54	1.6±0.11	0.0462	0.0542	0.002
Male	238.74±7.23	239.75±7.67	1.01±0.44	0.0354	0.0542	0.002
Female	239.00±7.13	240.10±6.21	1.1±0.92	0.0244	0.0453	0.001

DISCUSSION

The average age in our study was 48.68 years, with most pre-CMT values around 238.00 and post-CMT values near 239.42. Changes in CMT are small, averaging about 1.42, and the number of burns varies from 1902 to 2123, with a typical count of 2013.

Proliferative diabetic retinopathy (PDR) is one of the most common causes found in patients with diabetes, commonly in the working age group, which leads to legal blindness worldwide.[10] According to diabetic retinopathy studies or DRS, treatment of the PDR includes retinal photocoagulation in which the light is focused and absorbed by the retinal epithelium cells by the process of thermal coagulation. Through this process, the temperature of the tissue is increased and causes the protein denaturation and necrosis of the cells. Due to this denaturation of the cells, the blood oxygen supply is low, and the reduction of Vascular Endothelial Growth Factors (VEGF) leads to a reduction in PDR.[11,12,13,14]

In our study, the mean age of the subjects ranges from 32 to 65 years, with a mean of 48.68 years. A quasi-experimental study conducted in Lahore, Pakistan, showed that their mean age was 42.68±16.52 years. This age difference may mean their lifestyle modification was good as compared to the subjects of our study. Both studies show a significant increase in central macular thickness (CMT) after pan-retinal photocoagulation (PRP) for proliferative diabetic retinopathy (PDR). The first study reports a smaller mean increase of 1.42 μm, while the second study shows a larger mean increase of 11.5 μm, both statistically significant. Differences in treatment protocols and measurement methods may account for the variation in results, Similarly, we found that the majority of our participants were male as compared to females; however, in a similar study, it is in contrast to our findings, and another study from Pakistan also in contrast to our findings as females were in high proportion.[15,16] This may be due to gender bias. EDTRS reported that worsening of macular edema may increase vision loss in patients with pre-existing macular edema with the most PRP as compared to those without macular edema.[17,18,19,20,21] A non-randomized observation study also

revealed that the CMT was slightly greater in OCT after 1 month of follow-up.1 Another study by Astriviani et al. also reported that the thickness of the central macula was increased after two weeks of PRP1; we also found the same after a follow-up of one month. A similar finding was also reported by Watanachai et al, that after a single session of PRP, the central macular thickness was increased by about 24 micrometers in patients with PDR.24 Soman et al. also supported our findings after one month of follow after PRP the CMT increased.

Additionally, our results support the conclusions of Soman et al., who demonstrated that PRP leads to macular thickening even in the absence of CSME at baseline. This suggests that the mechanical and thermal impacts of the laser can induce structural changes in the macula despite pre-existing edema. Several studies have reported similar alterations in macular thickness following PRP treatment. Shahid et al, observed a similar increase in CMT, which aligns with our findings that the inflammatory response caused by laser therapy contributes to this thickening. In our study, pre-CMT values ranged from approximately 231.51 to 244.49, with a mean of 238.00, while post-CMT values ranged from 239.42 to 245.85, with a mean of 239.42. Changes in CMT ranged between 1.36 and 1.48, with a mean change of 1.42. The number of burns ranged from 1902 to 2123, with a mean of 2013. Table 2 shows that baseline CMT increased after one month in all groups: by 1.09 in those ≤50 years (p=0.001), and by 1.6 in those ≥50 years (p=0.002). Males experienced a 1.01 increase (p=0.002), while females had a 1.1 increase (p=0.001)25,7

In our study, the mean change in central macular thickness (CMT) was relatively minimal, at 1.42 μm, with significant increases observed across both age groups (≤50 years, $p = 0.001$; ≥50 years, $p = 0.002$) and genders (males, $p = 0.002$; females, $p = 0.001$) following treatment. The mean number of laser burns applied was 2013, suggesting a high-intensity photocoagulation protocol. In contrast, the second study reported a more pronounced increase in mean CMT, from 258.4 ± 30.7 μm at baseline to 269.9 ± 36.8 μm post-panretinal photocoagulation (PRP), with a mean increase of 11.5 ± 26.3 μm, which was also statistically significant ($p = 0.042$). Furthermore, normal distribution of data was confirmed both before ($W = 0.960$, $p = 0.445$) and after treatment ($W = 0.931$, $p = 0.103$) using the Shapiro-Wilk test.[22]

This study has several limitations that should be considered. Firstly, the sample size was relatively small, which may limit the generalizability of the findings to a larger population. Secondly, the short follow-up duration of one month may not fully capture the long-term changes in central macular thickness (CMT) after panretinal photocoagulation (PRP). Additionally, the study did not assess functional outcomes such as visual acuity changes or patient-reported quality of life, which are important in evaluating the clinical significance of anatomical changes. Furthermore, the study did not account for systemic factors such as glycemic control, blood pressure, or duration of diabetes, which could potentially influence macular thickness outcomes. Lastly, the absence of a control group limits the ability to attribute the observed changes solely to the PRP treatment.

CONCLUSION

We concluded that the central macular thickness (CMT) may increase after pan-retinal photocoagulation (PRP).

Conflict Of Interest: None to declare

Ethical Approval: The study was approved by the Institutional Review Board / Ethical Review Board vide ref No. PIMC/DMR/5 dated 31.03.2023.

Authors' Contributions:

Muhammad Asif: Concept, Design, Manuscript Editing, Manuscript Review

Ghazala Dure Huwaydah: Data acquisition, Data analysis, Statistical Analysis, Manuscript review

Fazal Nauman: Litrature search, Data analysis, Manuscript preparation, Manuscript editing, Manuscript review

Mujeeb ur Rehman: Data acquisition, Statistical analysis, Manuscript editing

Wasi Ullah: Literature search, Data acquisition, Data analysis, Statiscal analysis

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