ORIGINAL RESEARCH

Analysis of the Macular Region Following Panretinal Photocoagulation for the Treatment of Diabetic Retinopathy Using Optical Coherence Tomography

Haijing Cao, MM; Kai Wang, BD; Qing Pan, BD; Chaopeng Li, MM

ABSTRACT

Background • Diabetic retinopathy (DR) is the most prevalent microvascular complication of diabetes. Panretinal photocoagulation (PRP) is the established treatment for mitigating severe visual impairment resulting from proliferative DR.

Objective • This study aims to investigate the impact of PRP on the macular region in patients with DR, utilizing optical coherence tomography (OCT) for assessment.

Design • An experimental study was meticulously designed, implementing PRP as the primary intervention.

Setting • The investigation was conducted within the Department of Ophthalmology at the Affiliated Huaian No.1 People's Hospital, Huai'an, Jiangsu, China.

Participants • A total of 120 participants diagnosed with DR and undergoing treatment at our hospital were enrolled in the study.

Interventions • The participants were randomly assigned to either the control group (CG, n = 60) or the study group (SG, n = 60). The CG received conventional drug treatment involving oral iodized lecithin, while the SG received PRP. OCT was employed to monitor changes in macular fovea volume and macular retinal thickness.

Primary Outcome Measures • Evaluation criteria encompassed clinical efficacy, macular fovea volume, macular retinal thickness, IL-6 and VEGF levels, incidence of adverse reactions, and quality of life in both groups.

Results • The study resulted in a higher total effective rate in the SG (96.67%) compared to the CG (80.00%) ($\chi^2 = 8.09$, $P < .05$). Post-treatment, reductions were observed in macular fovea volume and macular retinal thickness, with significantly lower SG values than CG values ($P < .05$). Both serum IL-6 and VEGF levels exhibited reductions in both groups after treatment, with the SG displaying a more significant decrease compared to the CG ($P < .05$). The occurrence of adverse reactions significantly decreased in the SG relative to the CG ($P < .05$). Quality of life scores for the SG was notably elevated compared to the CG ($P < .05$).

Conclusions • PRP emerges as a highly valuable approach in the management of DR. It contributes to retinal thickness improvement within the macular region and inflammation reduction, and also enhances therapeutic outcomes, minimizes adverse reactions, and optimizes patients' quality of life. These findings warrant further clinical adoption and widespread promotion. (*Altern Ther Health Med.* 2023;29(8):324-328).

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INTRODUCTION

The annual incidence of diabetes mellitus has steadily increased each year, along with advancements in societal living standards and contemporary sedentary lifestyles becoming prevalent.[1] Diabetic retinopathy (DR) is among the most prevalent complications of diabetes mellitus and is a leading cause of low vision and blindness.[2] This condition significantly impacts patients' visual function and overall quality of life.[3] Consequently, the timely detection and treatment of DR assume paramount significance.

Panretinal Photocoagulation (PRP) remains the primary method for DR treatment.[4] PRP effectively delays retinal neovascularization formation while inducing atrophy and regression of pre-existing neovascularization. The coagulation impact of PRP leads to extensive cicatricial changes in the chorioretinal, which reduces oxygen demand and thins the retina. This alteration facilitates heightened oxygen availability to the inner retinal layer and promotes oxygen distribution across the posterior pole.[5] Positioned at the posterior pole of the eyeball and the temporal aspect of the optic nerve papilla, the macula, measuring a mere 3-4 mm, represents the region with the thinnest retinal layer and the highest visual sensitivity.[6]

Diabetic macular edema significantly impairs patients' visual function, and early postoperative PRP has the potential to impair this condition.[7] Therefore, close monitoring of alterations in the macular region after PRP is paramount for effectively managing DR patients during follow-up and guiding appropriate follow-up treatments. Over an extended duration, scholars have conducted numerous investigations into the pathogenesis of DR. Consensus holds that DR is rooted in a proliferative cellular mechanism, highlighting its deep connection with dysregulated cell proliferation.[8]

Cytokines emerge as key players in the regulation of cell proliferation, thus potentially influencing the inception and progression of retinal proliferative disorders.[9] Notably, vascular endothelial growth factor (VEGF) stands as the preeminent known mitogenic and angiogenic stimulator for endothelial cells, with its potent capacity to selectively induce vascular endothelial cell proliferation, participate in the formation of new blood vessels, and contribute to neovascularization.[10] VEGF assumes a central role in the intricate framework of DR-associated neovascularization.

Furthermore, cytokines may exert a substantial influence on the pathological progression of DR. Among these, interleukin-6 (IL-6), categorized as a proinflammatory cytokine, is secreted by activated T cells, mononuclear macrophages, fibroblasts, and specific tumor cells. It plays a critical role as a principal instigator of the acute phase response in instances of infection or trauma.[11] Notably, Yuuki et al.[12] have demonstrated the remarkable involvement of IL-6 in the pathological course of DR.

Optical coherence tomography (OCT) constitutes a non-invasive, high-resolution bio-tissue imaging technology that captures cross-sectional retinal scans. This technique enables the visual representation of retinal structure and quantitative assessment of retinal thickness and volume.[13] Therefore, conducting quantitative macular edema analysis post-photocoagulation via OCT holds significance in guiding the treatment of DR.[14]

This study explores the impact of PRP on the macular region using OCT imaging. Concurrently, we evaluated PRP's influence on inflammation, adverse reactions, and the quality of life for individuals affected by DR. Our research holds the potential to offer valuable insights into DR treatment strategies.

DATA AND METHODS

Study Design

A comprehensive cohort of 120 patients diagnosed with DR and admitted to our hospital between March 2021 and December 2022 was meticulously assembled. These participants were randomly allocated into two groups: the control group (CG, n = 60) and the study group (SG, n = 60). All patients provided informed consent before their inclusion in this study.

Inclusion and Exclusion Criteria

Inclusion criteria were as follows: (1) individuals with diabetes who displayed a diagnosis of DR imposing PRP; (2) individuals who strictly adhered to the criteria outlined in the Early Treatment of Diabetic Retinopathy Study; (3) individuals exhibited no antecedent history of ocular trauma or surgical interventions.

Exclusion criteria were as follows: A set of exclusion criteria was also applied: (1) Presence of other ocular disorders, including age-related macular degeneration, glaucoma, and optic nerve diseases; (2) Prior receipt of PRP therapy; (3) Contraindications to local anesthesia involving procaine; (4) DR patients concurrently afflicted with macular edema, vitreous hematoma, or retinal detachment; (5) Coexisting mental illness leading to an inability to collaborate with the prescribed treatment regimen; (6) Situated within the gestational or lactation periods.

Intervention Protocols

In the control group (CG), patients underwent conventional drug treatment involving oral administration of iodized lecithin (0.2 mg/time, thrice daily) from Daiichi Pharmaceutical Co., LTD., spanning a continuous 2-month course.

In contrast, participants in the study group (SG) underwent PRP utilizing an Argon krypton laser from the American Krypton Laser Company. Comprehensive photocoagulation was executed on the retina, employing krypton yellow light with a wavelength of 568.2 nm. The procedure commenced by identifying and targeting the afflicted blood vessels. In cases of macular edema, parameters were set as follows: spot size of 150 μm, energy set at 300 mJ, time interval of 0.2 s, with the rear pole of the retina addressed at 200 μm and mid-retinal adjustments set to 400 μm. The PRP treatment spanned four sessions, each conducted weekly, and required each spot to encompass 300 to 500 pulses.

Furthermore, laser parameters were adroitly tailored to enable combined photocoagulation. Treatment was carried out 1-4 times based on the extent of lesions, and a 7-day interval was observed between successive treatments.

Methods of Detection

Optical Coherence Tomography (OCT). The comprehensive examination of all patients was conducted by a consistent technician, employing the built-in posterior pole macular 3D scanning mode of the Topcon 3D OCT-2000 (Japan Topcon). In the macular region, the 3D scanning mode facilitated the evaluation of the mean retinal thickness within a 6 mm range and the neuroepithelial volume within the macular zone. The software integrated within the device automatically stratified and assessed these parameters, with technician validation of automatic stratification. The software conducted automated measurements and recorded the acquired data following necessary adjustments.

Serum IL-6 and VEGF Level Detection. A fasting elbow venous blood sample of 3 mL was obtained from each patient in the morning. Subsequent centrifugation at a speed of 4000 r/min for 15-20 minutes facilitated serum separation. The serum IL-6 and VEGF levels were assessed via enzyme-linked immunosorbent assay (ELISA) utilizing equipment from Shanghai Kehua Bio-Engineering Co., Ltd.

Clinical Efficacy Evaluation

Clinical efficacy was categorized into the following criteria: (1) Obvious Effect: Laser scar effectively enveloped retinopathy, leading to complete lesion resolution; (2) Effective: retinopathy condition exhibited improvement, resulting in partial lesion subsidence; (3) ineffective: Lesion remained unchanged or displayed a tendency towards exacerbation.

The total effective rate was calculated as the sum of the significant effective rate and the effective rate, offering a comprehensive gauge of treatment outcomes.

Total effective rate = significant effective rate + effective rate

Observational Parameters

Comparative Clinical Efficacy. A thorough evaluation of clinical efficacy was conducted for both groups three months post-treatment.

Macular Fovea Volume and Macular Retinal Thickness. Precise assessment of macular fovea volume and macular retinal thickness was performed in both groups before and three months after the treatment.

Serum IL-6 and VEGF Levels. Serum levels of IL-6 and VEGF were quantified before treatment and three months post-treatment in both groups.

Incidence of Adverse Reactions. The occurrence of adverse reactions, including retinal hemorrhage, anaphylactic reactions, gastrointestinal discomfort, macular edema, and ophthalmodynia, was documented three months after treatment in both groups.

Quality of Life Evaluation. Utilizing the Short Form 36 Health Survey Questionnaire (SF-36),[15] the quality of life for all patients was comprehensively assessed three months post-treatment. The questionnaire covered eight domains: physiological function, social function, emotional function, physical pain, mental health, vitality, and general health. Scores ranged up to 100 points, with higher scores indicative of an improved quality of life.

Statistical Analysis

Data was processed using SPSS 19.0 software (IBM, Armonk, NY, USA). Count data were presented as n (%) and analyzed using the Chi-square test to compare group differences. Measurement data were exhibited as means ± standard deviation ($\bar{x} \pm s$), and intergroup comparisons were executed via the t test. Significance was established at $P < .05$.

RESULTS

Demographic Characteristics of Patient Cohorts

After careful examination, no notable disparity emerged in the demographic profiles of the two groups ($P > .05$), highlighting their comparability, as represented in Table 1.

Clinical Efficacy Comparison

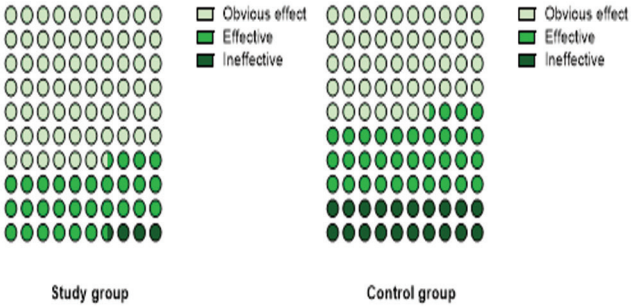
The total effective rate in the SG (96.67%) was higher compared to the CG (80.00%) ($\chi^2 = 8.09$, $P < .05$), as shown in Figure 1.

Table 1. General Data of Patients in Both Groups

Items	Control Group (n = 60)	Study Group (n = 60)	*P* value
Gender (male/female, n)	35/25	34/26	>.05
Average Age (years, $\bar{x} \pm s$)	40.36 ± 4.47	40.30 ± 4.51	>.05
Average course of disease (years, $\bar{x} \pm s$)	6.83 ± 1.24	6.80 ± 1.26	>.05

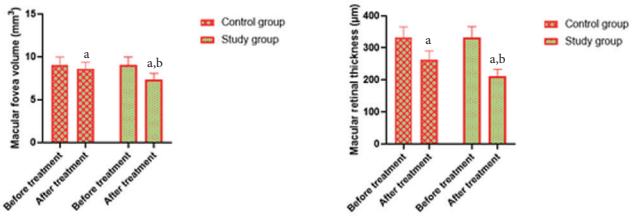
Note: General data of patients in both groups were compared. $\bar{x} \pm s$: mean standard deviation.

Figure 1. Comparison of clinical efficacy in both groups.



Note: The figure illustrates the comparison of clinical efficacy between the Control Group (CG) and Study Group (SG). The total effective rate in the SG (96.67%) was significantly higher compared to the CG (80.00%) ($\chi^2 = 8.09$, $P < .05$). This visual representation highlights the favorable outcomes of the Study Group in terms of clinical efficacy.

Figure 2. Comparison of macular fovea volume and macular retinal thickness in both groups before and 3 months after treatment.



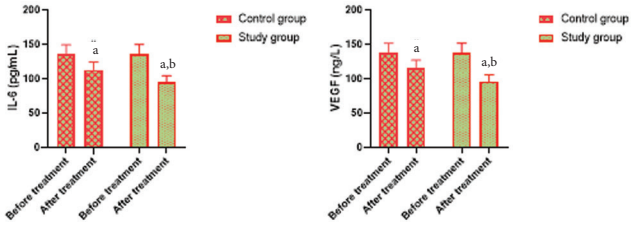
[a]$P < .05$, compared to before treatment
[b]$P < .05$, compared to the control group

Macular Fovea Volume and Macular Retinal Thickness Assessment

In the CG, the pre-treatment macular fovea volume measured (9.06 ± 0.92) mm³, with a corresponding macular retinal thickness of (332.69 ± 33.26) μm. Similarly, the SG presented a pre-treatment macular fovea volume of (9.05 ± 0.93) mm³ and a macular retinal thickness of (332.72 ± 33.32) μm. Before treatment initiation, no statistically significant differences were observed in macular fovea volume and macular retinal thickness between the two groups ($P < .05$ and $P < .05$, respectively).

Following treatment, notable alterations were evident. In the control group, post-treatment measurements indicated a decrease in macular fovea volume to (8.54 ± 0.83) mm³ and a corresponding reduction in macular retinal thickness to (264.23 ± 26.41) μm. Parallel observations were recorded in the study group, with post-treatment macular fovea volume measuring (7.32 ± 0.73) mm³ and macular retinal thickness decreasing to (211.61 ± 21.18) μm. Remarkably, both macular fovea volume and macular retinal thickness exhibited reductions in both groups post-treatment ($P < .05$ and $P < .05$, respectively), and the study group displayed lower values in

Figure 3. Comparison of serum levels of inflammatory factors in both groups before and 3 months after treatment.



#$P < .05$, compared to before treatment
*$P < .05$, compared to the control group.

Abbreviations: IL-6, interleukin-6. VEGF, vascular endothelial growth factor.

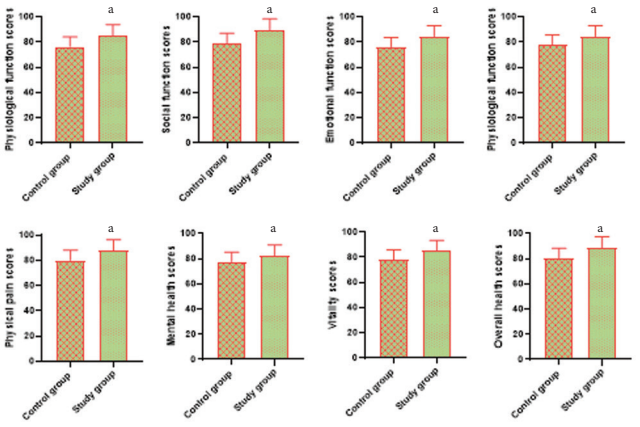
Table 2. Occurrence of Adverse Reactions in Both Groups.

Adverse Reactions	Control Group (n = 60)	Study Group (n = 60)
Retinal Hemorrhage	3	1
Anaphylactic Reaction	3	0
Gastrointestinal Discomfort	2	0
Macular Edema	2	1
Ophthalmodynia	1	1
Total Incidence Rate [n (%)]	11 (18.33%)	3 (5.00%)
χ^2	5.18	
P value	<.05	

Note: The table illustrates the occurrence of adverse reactions in both groups.

Abbreviations: n, Number of patients observed; χ^2, Chi-square test statistic, used to assess the association between categorical variables; *P* value, Statistical significance level indicating the likelihood of observing results by chance.

Figure 4. Comparison of quality of life in each dimension between both groups 3 months after treatment.



[a]indicates statistical significance ($P < .05$), emphasizing dimensions where a significant difference was observed between the two groups.

Note: The figure depicts the comparison of quality of life across various dimensions between the Control Group (CG) and Study Group (SG) at the 3-month mark post-treatment.

comparison to the control group ($P < .05$ and $P < .05$, respectively), as displayed in Figure 2.

Serum Inflammatory Factors Analysis

The pre-treatment serum IL-6 level in CG stood at (136.35 ± 13.42) pg/mL, while the corresponding serum VEGF level was recorded as (138.25 ± 13.87) ng/L. Similarly, SG presented with a pre-treatment serum IL-6 level of (136.54 ± 13.68) pg/mL and a serum VEGF level of (138.29 ± 13.78) ng/L. Before treatment commencement, no noticeable disparities emerged in serum IL-6 and VEGF levels between the two groups ($P < .05$ and $P < .05$, respectively).

Upon treatment completion, remarkable shifts were observed. In CG, post-treatment analysis revealed a decline in serum IL-6 levels to (113.27 ± 11.43) pg/mL, and serum VEGF levels reduced to (115.43 ± 12.03) ng/L. In parallel, SG displayed post-treatment serum IL-6 levels of (95.17 ± 9.56) pg/mL and serum VEGF levels of (96.38 ± 9.73) ng/L. Notably, both inflammatory factor levels demonstrated notable decreases in both groups post-treatment ($P < .05$ and $P < .05$, respectively), with the study group showing more pronounced reductions compared to the control group ($P < .05$ and $P < .05$, respectively), as illustrated in Figure 3.

Incidence of Adverse Reactions

A notable difference in the incidence of adverse reactions observed between SG and the CG, with occurrences of 5.00% and 18.33%, respectively ($P < .05$). A comprehensive representation is presented in Table 2.

Quality of Life Assessment

The study group exhibited notable superiority across diverse dimensions of quality of life when compared against the control group: (1) Physiological Function Score: The SG displayed a score of (85.43 ± 8.54), distinctly higher than the CG score of (76.54 ± 7.63) ($P < .05$); (2) Social Function Score: The SG achieved a score of (89.64 ± 8.92), surpassing the CG score of (79.28 ± 7.93) ($P < .05$); (3) Emotional Function Score: A distinct elevation was observed in the SG, with a score of (84.61 ± 8.41), contrasted with the CG score of (76.21 ± 7.58) ($P < .05$); (4) Physical Function Score: The SG demonstrated a score of (84.59±8.51), in contrast to the CG score of (77.68 ± 8.02) ($P < .05$); (5) Physical Pain Score: The SG's score of (87.64 ± 8.72) outperformed the CG score of (80.04 ± 8.01) ($P < .05$); (6) Mental Health Score: The SG achieved a score of (82.69±8.31), surpassing the CG score of (77.59 ± 7.78) ($P < .05$); (7) Vitality Score: The SG's score of (84.97 ± 8.51) outshone the CG score of (78.03 ± 7.81) ($P < .05$); (8) Overall Health Score: The SG recorded a score of (88.69 ± 8.87), notably higher than the CG score of (80.32 ± 8.06) ($P < .05$), details are visually depicted in Figure 4.

DISCUSSION

The exact cause of DR is not fully understood yet. Most scholars believe it is closely linked to the inflammatory response, oxidative stress response, hyperglycemia, hemodynamic disorders, and other factors of body function.[19] Interestingly, VEGF is expressed at lower levels in normal retinal pigment epithelial cells and vascular endothelial cells, but its expression is significantly higher in patients with DR.[20] The underlying cause behind this issue is usually retinal hypoxia, which can result in exudation, bleeding, edema, and other related issues. Additionally, VEGF can attach to specific receptors on cell surfaces, encouraging the migration and growth of endothelial cells and the formation of new blood vessels. This process can ultimately lead to irreversible damage to visual function.[21]

The SG exhibited an elevated total effective rate in this study compared to the CG. After treatment, the SG demonstrated reduced macular fovea volume and macular retinal thickness relative to the CG. Remarkably, a study conducted by Ahsan Mukhtar et al.[16] supported these findings by demonstrating the ability of panretinal photocoagulation to diminish macular retinal thickness in individuals with proliferative DR.

The incidence of adverse reactions in the SG was notably diminished when contrasted with the CG. Concurrently, the quality-of-life scores within the SG demonstrated improvements when compared to the CG. These results signify that PRP holds the potential to expedite patient recovery, foster optimal therapeutic outcomes, and enhance overall quality of life. These findings align with prior scholarly research.[17] However, Jelena et al.[18] have demonstrated that laser treatment for DR can lead to a decline in certain aspects of patients' perceived vision-related quality of life. This disparity might be attributed to our comparatively shorter follow-up duration, during which our patients did not undergo sufficient time to experience a deterioration in visual acuity after PRP treatment.

IL-6 is a bioactive factor that impacts target organs through various modes, including endocrine, secretory, and paracrine actions.[22] It is generated by epithelial cells, mononuclear phagocytes, and effector lymphocytes outside the eye, as well as by the epithelial cells and ciliary bodies within the retina and cornea.[23] IL-6 has the capability to hinder the generation and progression of vascular endothelial cells, trigger inflammation, harm vascular endothelial cells, and collaboratively work with VEGF to promote microvascular occlusion and neovascularization.[24]

In our study, serum IL-6 and VEGF levels in the SG were observed to decrease compared to the CG after treatment. This finding suggests that PRP might effectively reduce retinal vascular leakage, lower VEGF levels, and hinder vascular regeneration.[25] At the same time, PRP has inherent properties that can sterilize and dampen inflammation.[26] These findings underscore the potential of PRP in mitigating retinal vascular issues, reducing VEGF levels, and dampening inflammation.

Study Limitations

There are certain limitations to be acknowledged. The relatively short follow-up duration may not capture longer-term changes in visual acuity or quality of life. Additionally, the sample size could impact the generalizability of the results, and further investigations with larger and more diverse populations are warranted. The absence of detailed analysis of individual patient characteristics, such as diabetes control levels, may also influence the overall interpretation of the findings. The insights garnered from this study open avenues for future research to explore extended follow-up periods and larger, diverse cohorts, providing a deeper understanding of PRP's long-term impact on diabetic retinopathy management.

CONCLUSION

In conclusion, this study elucidated the multifaceted impact of PRP in managing diabetic retinopathy. The findings revealed that PRP could reduce inflammation, optimize therapeutic outcomes, mitigate adverse reactions, and elevate patients' overall quality of life beyond its capacity to enhance retinal thickness in the macular region. This collective impact underscores the significance of PRP's role, warranting its further integration and promotion within clinical practice.

CONFLICT OF INTEREST

The authors declare to have no conflict of interest.

DATA AVAILABILITY STATEMENT

The supporting data is available upon request to the corresponding author.

AUTHORS' CONTRIBUTION

All authors contributed equally, read and approved the final manuscript.

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