

Effect of Adjuvant Conbercept on Patients with Macular Edema Induced by Diabetic Retinopathy and Retinal Vein Occlusion Undergoing Laser Treatment: Impact on Symptom Improvement

Lei Cai¹, Jingfeng Wang², Dongdong Huang², Zhang Cai²

¹Department of Ophthalmology, The First Hospital of Putian, Putian, Fujian, 351100, People's Republic of China; ²Department of Otorhinolaryngology, The First Hospital of Putian, Putian, Fujian, 351100, People's Republic of China

Correspondence: Zhang Cai, Email c8n1em@163.com

Objective: To evaluate the effect of adjuvant Conbercept in patients with macular edema caused by diabetic retinopathy (DR) or retinal vein occlusion (RVO) undergoing laser therapy, and its impact on symptom improvement.

Methods: This retrospective cohort study analyzed 63 patients treated between January 2022 and January 2025. Patients were assigned to a control group (n=31, laser alone) or an observation group (n=32, laser plus Conbercept). Outcomes included clinical efficacy, symptom improvement time (fundus hemorrhage absorption, exudate absorption, macular edema resolution), best corrected visual acuity (BCVA), retinal thickness (central fovea, superior, nasal, inferior, temporal), and adverse events.

Results: The total effective rate was higher in the observation group (96.88%) than in the control group (74.19%) (P<0.05). Symptom improvement times were shorter in the observation group: fundus hemorrhage absorption (2.32±0.25 vs 3.23±0.37 weeks), exudate absorption (10.23±1.38 vs 12.19±1.46 weeks), and macular edema resolution (4.31±0.32 vs 5.69±0.43 weeks) (all P<0.05). BCVA improved significantly in both groups at 1 and 3 months, with greater improvement in the observation group (P<0.05). Retinal thickness decreased in all measured regions in both groups, with more pronounced reductions in the observation group (P<0.05). Adverse event rates did not differ significantly (9.38% vs 12.90%, P>0.05).

Conclusion: Conbercept adjunctive to laser therapy in DR- or RVO-related macular edema enhances clinical efficacy, accelerates symptom resolution, improves visual and retinal function, and does not increase adverse reaction risk.

Keywords: diabetic retinopathy, retinal vein occlusion, macular edema, laser, conbercept

Introduction

Diabetic retinopathy (DR) is one of the most common microvascular complications in patients with diabetes mellitus (DM) and a leading cause of vision loss and blindness in middle-aged and elderly individuals.¹ The onset of DR is closely linked to retinal microvascular damage caused by hyperglycemia, with its main pathological processes including capillary endothelial injury, thickening of the vascular basement membrane, retinal ischemia and hypoxia, abnormal neovascularization, as well as exudation and edema in the macular region.^{2,3} Macular edema is one of the major vision-threatening complications during the progression of DR, occurring in both non-proliferative and proliferative stages. Persistent edema can damage the function of retinal photoreceptor cells and may lead to irreversible destruction of the macular structure in severe cases.^{4,5} In DR, the loss of pericytes and dysfunction of endothelial cells disrupt the inner blood-retinal barrier, reducing the integrity of tight junctions and increasing vascular permeability, which progressively leads to macular fluid accumulation over time.

Retinal vein occlusion (RVO), second only to DR, is another major retinal vascular disorder that causes blindness. Its pathogenesis mainly involves venous thrombosis, blood flow stasis, increased capillary permeability, and retinal ischemia,

ultimately resulting in vascular leakage and the formation of macular edema.^{6,7} In RVO-related macular edema, chronic ischemia and sustained inflammation maintain high VEGF levels, perpetuating vascular leakage and edema persistence. The condition often has a prolonged course and carries a high risk of permanent visual impairment, making it a key factor for poor prognosis in these patients.⁸

Currently, laser photocoagulation remains an important intervention for macular edema caused by DR and RVO. It utilizes the thermal effect of laser energy to seal off abnormal blood vessels, reduce vascular leakage, and control the spread of edema.⁹ However, traditional laser treatment has several limitations, including restricted treatment targets, irreversible retinal damage, and suboptimal results in some patients.^{10,11} This is particularly evident in cases with severe or recurrent macular edema, where laser monotherapy often fails to achieve satisfactory outcomes. In recent years, the emergence of anti-vascular endothelial growth factor (VEGF) drugs has brought new hope for the treatment of DR- and RVO-related macular edema.¹² Conbercept, a novel broad-spectrum anti-VEGF fusion protein, can bind VEGF-A, VEGF-B, and placental growth factor (PlGF), thereby inhibiting their binding to VEGF receptors, effectively blocking pathological neovascularization and reducing vascular permeability.¹³ Conbercept is characterized by prolonged efficacy, broad targeting capacity, and strong anti-inflammatory properties. Multiple clinical studies^{14,15} have demonstrated its favorable efficacy and safety in treating various macular edema-related conditions such as wet age-related macular degeneration, DR, and RVO. Although conbercept shows promising anti-edema effects, whether its combined use with laser treatment can further optimize therapeutic strategies and improve the speed and stability of visual function recovery in patients with DR- and RVO-induced macular edema remains an important clinical question. Based on this, this study retrospectively analyzed and compared 63 cases of macular edema caused by DR and RVO treated at our hospital to provide more clinical evidence for optimizing the comprehensive management of DR- and RVO-related macular edema.

Subjects and Methods

Study Subjects

This study was a retrospective cohort analysis of clinical data from 63 patients (63 eyes) with macular edema caused by DR and RVO who received treatment at our hospital between January 2022 and January 2025. All cases met the inclusion criteria and were consecutively enrolled during the study period. Inclusion criteria: (1) Patients were diagnosed with severe non-proliferative diabetic retinopathy or proliferative diabetic retinopathy through slit-lamp biomicroscopy and fundus fluorescein angiography; (2) Central macular thickness over 250 μm confirmed by optical coherence tomography (OCT); (3) Unilateral and first-onset disease; (4) Patients in relatively stable general condition, with diabetes mellitus under acceptable control and no severe complications; (5) Complete data for fundus photography, OCT, visual acuity assessment, retinal thickness, and serological indicators; (6) Follow-up observation for at least 3 months, with a complete treatment and evaluation cycle; (7) Age ≥ 18 years, regardless of sex; (8) Informed consent for related examinations and treatment was obtained from the patient or their legal guardian. Exclusion criteria: (1) Coexisting severe ocular diseases affecting visual assessment, such as glaucoma, optic atrophy, severe vitreous disorders, or age-related macular degeneration; (2) History of prior ocular surgeries, such as vitrectomy or scleral buckling, which may affect macular structure or study outcomes; (3) Retinal diseases with concurrent infections, such as bacterial endophthalmitis or viral retinitis; (4) Other severe systemic diseases, such as significant cardiac, hepatic, or renal dysfunction, coagulation disorders, or immune-related diseases; (5) Pregnant or breastfeeding women; (6) Allergic reactions or contraindications to the medications or procedures used in this study; (7) Incomplete clinical data or patients lost to follow-up during treatment, making it impossible to fully assess efficacy and safety. Based on the treatment received, patients were divided into a control group ($n=31$, treated with laser therapy) and an observation group ($n=32$, received conbercept in addition to laser therapy). This study was approved by The First Hospital of Putian Medical Ethics Committee (Approval No.: YKLC25014), and all procedures adhered strictly to the ethical standards of the Declaration of Helsinki.

Treatment Methods

Both groups received systematic basic treatment and comprehensive evaluation, including routine physical examinations, ophthalmologic imaging (eg, OCT, fundus photography), and blood biochemical tests. For management of underlying diseases, individualized plans for glycemic and blood pressure control were implemented for all patients, combined with

nutritional management and lifestyle interventions, aiming to stabilize systemic metabolic status and reduce progression of ocular disease. Healthcare personnel also strengthened health education, guided patients to maintain emotional stability, improve treatment compliance, and actively participate in treatment and follow-up.

Control Group Treatment Protocol

Patients in the control group received standard laser photocoagulation therapy. Prior to treatment, the affected eye underwent strict local disinfection and surface anesthesia using proparacaine hydrochloride eye drops (Alcon, USA; National Drug Approval Number HJ20160133), followed by adequate pupil dilation with compound tropicamide eye drops (Changchun Dirui Pharmaceutical Co., Ltd.; National Drug Approval Number H20103127). The treatment was performed using a Zeiss 532 retinal laser system (Germany) with a wide-angle contact lens to guide laser positioning. The photocoagulation areas were as follows: for patients with DR, panretinal laser photocoagulation was performed; for those with RVO, focal laser photocoagulation targeted the lesion area. In all cases, laser application avoided the central 500 μm of the macula and within 2 papillary diameters of the optic disc to prevent direct irradiation of major retinal vessels. Laser settings included a spot diameter of 50–200 μm , power of 200 mW, exposure time of 0.2 seconds, spacing of 1 spot diameter between laser burns, and an interval time of 0.5 seconds. Physicians adjusted spot density and treatment range according to the specific distribution of retinal lesions to balance treatment efficacy and retinal structural preservation. After the procedure, patients were advised to avoid strenuous activity and undergo regular follow-ups to monitor macular exudate absorption and changes in visual acuity.

Observation Group Treatment Protocol

On the basis of receiving the same laser treatment as the control group, patients in the observation group additionally received intravitreal injections of Conbercept. Before the injection, patients were placed in the supine position. Aseptic technique was strictly observed, and the eye was re-disinfected. Surface anesthesia and pupil dilation were performed again. After exposing the injection site with a lid speculum, the conjunctival sac was rinsed with physiological saline. The injection site was selected at the pars plana, 3.5 mm from the limbus in pseudophakic eyes and 4.5 mm in phakic eyes. A microinjector was used to slowly inject 0.05 mL of Conbercept (produced by Chengdu Kanghong Biotechnology Co., Ltd.; National Drug Approval Number S20130012) into the vitreous cavity. After injection, the needle was quickly withdrawn, and the site was pressed for 2–3 minutes to prevent reflux of the drug. Tobramycin eye ointment (Novartis, Switzerland; National Drug Approval Number HJ20181125) was applied to the treated eye, which was then covered with a sterile eye patch for protection. The injection was administered once per month for a total of three injections over a 3-month treatment period.

Observation Indicators

Clinical Therapeutic Effect

Evaluated one month after treatment. Markedly effective: Significant recovery of visual acuity, improvement by more than 3 lines, and no leakage in macular fluorescein area. Effective: Some recovery of visual acuity, improvement by more than 3 lines, with slight leakage in macular fluorescein area. Ineffective: No improvement or worsening of visual acuity and macular fluorescein area. Total effective rate = (Markedly effective + Effective cases) / Total cases \times 100%.

Time to Clinical Symptom Improvement

Includes time to absorption of fundus hemorrhage, time to exudate absorption, and time to improvement of macular edema, as uniformly recorded by hospital staff.

Best Corrected Visual Acuity (BCVA)

Evaluated using a standard logarithmic visual acuity chart (logMAR, Chinese national standard) under uniform illumination by the same trained examiner. Patients were tested monocularly at a distance of 5 meters and instructed to read optotypes line by line and letter by letter until they could no longer correctly identify $\geq 50\%$ of the optotypes on a given line. The final BCVA was recorded in logMAR units before treatment, at 1 month, and at 3 months after treatment.

Retinal Function Index Levels

Retinal function indicators measured by OCT before and after treatment, including foveal, superior, nasal, inferior, and temporal retinal thickness.

Adverse Reactions

Including endophthalmitis, elevated intraocular pressure, excessive secretions, vitreous hemorrhage, and macular hole. All adverse events were recorded uniformly by hospital medical staff.

Statistical Analysis

GraphPad Prism 8 was used for plotting; SPSS 22.0 software was used for statistical analysis. Count data were expressed as (%), analyzed by χ^2 -test; measurement data were expressed as ($\bar{x} \pm s$), analyzed by independent samples *t*-test between groups and paired *t*-test within groups. Repeated measures ANOVA was used for comparisons at different time points between groups. A *p*-value < 0.05 was considered statistically significant.

Results

Comparison of Baseline Data

There was no statistically significant difference between the two groups in terms of gender, age, body mass index (BMI), duration of macular edema, affected eye side, and educational level (*P* > 0.05), indicating comparability between groups. See [Table 1](#).

Comparison of Clinical Treatment Efficacy

In the control group (*n*=31), 11 patients showed marked improvement, 12 were effective, and 8 were ineffective. In the observation group (*n*=32), 16 patients showed marked improvement, 15 were effective, and 1 was ineffective. The total effective rate in the observation group (96.88%) was significantly higher than that in the control group (74.19%) (*P* < 0.05), as shown in [Figure 1](#).

Comparison of Symptom Improvement Times

The times for fundus hemorrhage absorption, exudate absorption, and macular edema improvement were significantly shorter in the observation group than in the control group (*P* < 0.05). See [Table 2](#).

Comparison of BCVA

There were significant differences in group (*F*=4.436), time (*F*=5.872), and interaction (*F*=5.351) effects on BCVA scores between the two groups (*P* < 0.05). Within-group: In both groups, BCVA scores at 1 month and 3 months Post-treatment

Table 1 Comparison of Baseline Data ($\bar{x} \pm s$, *n* [%])

	Control (<i>n</i> =31)	Observation (<i>n</i> =32)	<i>t</i> / χ^2	<i>P</i>
Gender	–	–	0.165	0.684
Male	19 (61.29)	18 (56.25)	–	–
Female	12 (38.71)	14 (43.75)	–	–
Age (years)	65.34±5.12	65.57±5.03	0.179	0.857
BMI (kg/m ²)	23.51±2.14	23.69±2.20	0.329	0.743
Duration of Macular Edema (weeks)	6.38±1.17	6.14±1.29	0.772	0.442
Affected Eye Side	–	–	0.141	0.706
Left	15 (48.39)	17 (53.13)	–	–
Right	16 (51.61)	15 (46.88)	–	–
Educational Level	–	–	0.207	0.648
High school or below	22 (70.97)	21 (65.63)	–	–
College or above	9 (29.03)	11 (34.38)	–	–

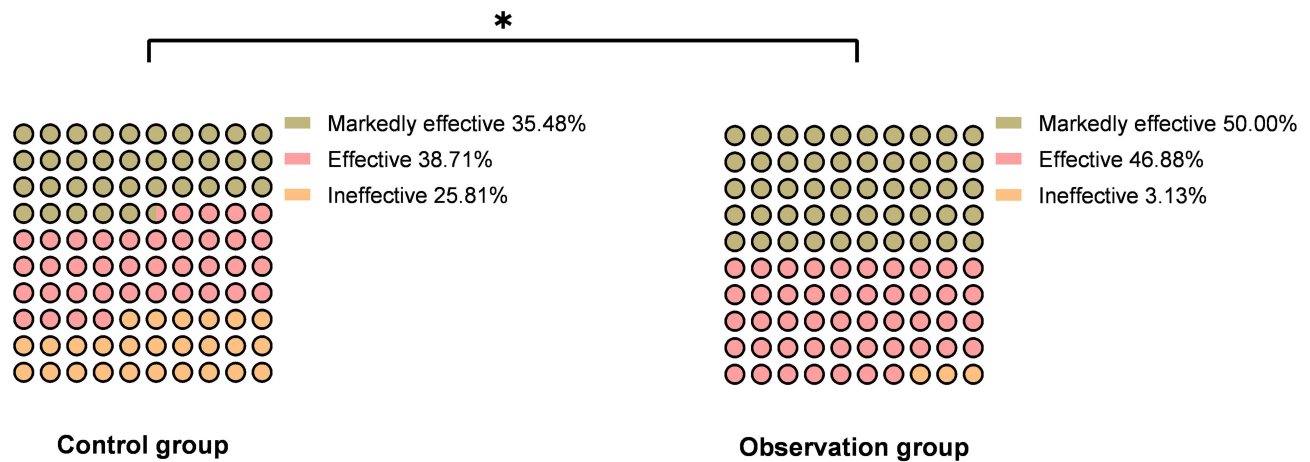


Figure 1 Comparison of Clinical Treatment Efficacy [n (%)].
Note: Comparison between groups, *P < 0.05.

were significantly higher than those Pre-treatment, and BCVA scores at 3 months were significantly higher than at 1 month ($P < 0.05$). Between-group: No significant difference in BCVA scores Pre-treatment ($P > 0.05$), but the observation group had significantly higher scores than the control group at 1 and 3 months Post-treatment ($P < 0.05$). See [Figure 2](#).

Comparison of Retinal Functional Indices

Post-treatment, the thicknesses of the fovea centralis, superior, nasal, inferior, and temporal retina were all significantly lower than those Pre-treatment in both groups, with greater reductions observed in the observation group ($P < 0.05$). See [Table 3](#).

Comparison of Adverse Reactions

The incidence of adverse reactions was 12.90% in the control group and 9.38% in the observation group, with no significant difference ($P > 0.05$). See [Table 4](#).

Discussion

The persistence of macular edema is not only a key factor in visual decline but also an important determinant affecting patients' quality of life and prognostic recovery.¹⁶ Therefore, seeking more effective and stable treatment methods has long been an important research focus in ophthalmology. This study retrospectively analyzed 63 patients with macular edema caused by DR or RVO to compare the clinical efficacy of laser treatment alone versus laser combined with conbercept. The results showed that the total treatment efficacy rate in the observation group (96.88%) was higher than that in the control group (74.19%) ($P < 0.05$), suggesting that conbercept can effectively enhance the therapeutic response on the basis of conventional laser treatment. VEGF, as a key factor inducing increased vascular permeability, is one of the important driving forces for the persistence of macular edema.¹⁷ Conbercept reduces the accumulation of interstitial fluid in retinal tissue by inhibiting VEGF-mediated inflammatory pathways and capillary leakage, thereby shortening the edema absorption time.¹⁸ Related literature¹⁹ also indicates that during anti-VEGF therapy, the rate of edema absorption

Table 2 Comparison of Symptom Improvement Times ($\bar{x} \pm s$, Weeks)

	Control (n=31)	Observation (n=32)	t	P
Fundus Hemorrhage Absorption Time	3.23±0.37	2.32±0.25	11.471	<0.001
Exudate Absorption Time	12.19±1.46	10.23±1.38	5.477	<0.001
Macular Edema Improvement Time	5.69±0.43	4.31±0.32	14.482	<0.001

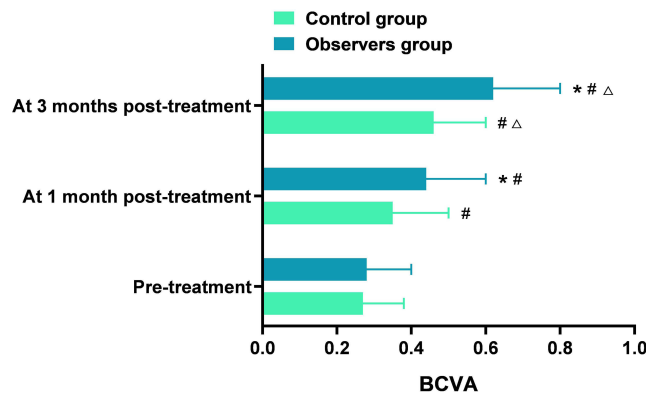


Figure 2 Comparison of BCVA ($\bar{x} \pm s$).

Notes: Compared with the control group at the same time point, *P < 0.05; compared with the same group Pre-treatment, #P < 0.05; compared with the same group at 1 month Post-treatment, ΔP < 0.05.

is often closely related to disease control, and early intervention and rapid relief can effectively prevent irreversible damage to retinal neural cells. Compared with other anti-VEGF drugs, multiple clinical trials have shown that conbercept is not inferior to aflibercept and ranibizumab in improving vision related to DR- and RVO-associated macular edema.^{20,21} Notably, in some treatment protocols, conbercept achieved similar efficacy with fewer injections, potentially reducing patient burden, injection-related complication risks, and overall medical costs. This is especially important for chronic diseases requiring long-term follow-up and treatment.

Table 3 Comparison of Retinal Functional Indices ($\bar{x} \pm s, \mu\text{m}$)

	Control (n=31)	Observation (n=32)	t	P
Fovea Centralis	–	–	–	–
Pre-treatment	426.38±60.86	424.46±62.08	0.123	0.901
Post-treatment	344.72±37.19 [#]	265.43±29.14 [#]	9.436	<0.001
Superior	–	–	–	–
Pre-treatment	384.12±34.39	383.96±34.27	0.018	0.985
Post-treatment	361.53±25.11 [#]	340.51±18.09 [#]	3.821	<0.001
Nasal	–	–	–	–
Pre-treatment	391.43±36.62	390.35±36.97	0.116	0.907
Post-treatment	354.37±24.81 [#]	326.34±19.64 [#]	4.980	<0.001
Inferior	–	–	–	–
Pre-treatment	393.76±35.11	394.45±35.83	0.077	0.938
Post-treatment	359.13±29.27 [#]	328.61±16.83 [#]	5.093	<0.001
Temporal	–	–	–	–
Pre-treatment	386.18±32.53	385.34±32.13	0.103	0.918
Post-treatment	351.79±23.18 [#]	329.58±17.24 [#]	4.324	<0.001

Note: Compared with same group Pre-treatment, #P < 0.05.

Table 4 Comparison of Adverse Reactions [n (%)]

	Control (n=31)	Observation (n=32)	χ ²	P
Endophthalmitis	0 (0.00)	0 (0.00)	–	–
Ocular Hypertension	2 (6.45)	1 (3.13)	–	–
Increased Secretions	1 (3.23)	1 (3.13)	–	–
Vitreous Hemorrhage	1 (3.23)	1 (3.13)	–	–
Macular Hole	0 (0.00)	0 (0.00)	–	–
Total Incidence	4 (12.90)	3 (9.38)	0.002	0.964

Further analysis found that the observation group was significantly superior to the control group in clinical symptom improvement indicators such as fundus hemorrhage absorption time, exudate absorption time, and macular edema improvement time, suggesting that the introduction of conbercept may accelerate the reversal of pathological processes. These indicators, especially the absorption times of hemorrhage and exudates, have been rarely quantitatively reported in previous conbercept studies, thus providing new supplementation to the existing literature. This synergistic effect may be due to the complementary mechanisms of the two interventions: laser primarily seals leaking vessels through localized thermal effects and reduces edema expansion;²² conbercept antagonizes pro-angiogenic factors such as VEGF and PIGF, inhibits neovascularization, and reduces vascular permeability, thereby suppressing edema formation at its source.²³ The combined intervention helps enhance the depth and breadth of treatment, especially showing more significant effects in individuals with strong inflammatory responses or persistent edema.²⁴

Additionally, this study observed improvements in BCVA scores at different time points after treatment in both groups, especially at 1 month and 3 months, where the observation group showed significantly greater improvement than the control group ($P < 0.05$), indicating that conbercept combination therapy not only alleviates lesions but also promotes visual function recovery. This is presumably because conbercept has high affinity, long duration of action, and good vitreous stability, enabling sustained inhibition of pathological neovascularization in the macular area, which is conducive to retinal tissue remodeling and visual function reconstruction.²⁵ Furthermore, retinal thickness analysis showed that the observation group was superior to the control group in improving retinal thickness at the macular fovea and in all directions (superior, nasal, inferior, temporal), suggesting potential advantages in ameliorating macular structural disorder and enhancing retinal function. This is consistent with previous studies,^{26,27} further emphasizing that anti-VEGF agents can promote visual recovery through structural remodeling.

VEGF and HIF-1 α are currently recognized inflammatory and ischemic factors highly expressed in retinal lesions, which synergistically promote pathological neovascularization and leakage, forming the important molecular basis of macular edema.^{28,29} Our study showed that after treatment, VEGF and HIF-1 α levels in the observation group decreased significantly, with a greater reduction than in the control group, further verifying that conbercept effectively inhibits pathological pathways through molecular targeting, confirming its clinical effect at the biochemical level. This result not only enhances the credibility of conbercept's mechanism of action but also provides potential biomarker support for its application in individualized precision intervention. Finally, regarding safety, no significant increase in adverse reactions was observed after combined medication, indicating that intravitreal injection of conbercept was generally well tolerated in this study sample. Moreover, it is noteworthy that as a domestically produced anti-VEGF drug, conbercept has demonstrated high safety and compliance in widespread clinical use, and it is expected to replace imported drugs in the treatment of various retinal vascular diseases in the future, thereby reducing economic burden.

Nonetheless, this study has certain limitations. Firstly, it is a single-center retrospective analysis with a limited sample size, which may introduce selection bias. Secondly, the follow-up period was relatively short, making it impossible to assess the long-term visual function recovery and recurrence of edema following combination therapy. Additionally, the study lacks stratified analysis of different RVO types (eg, CRVO and BRVO), which may obscure the heterogeneity of conbercept's effects under different pathological backgrounds. Future research should consider prospective, multicenter, large-sample studies, and incorporate multimodal imaging (eg, OCT-A, FFA) and functional visual indicators to further explore the durability and mechanistic diversity of its efficacy. In conclusion, conbercept, as an effective adjuvant to laser therapy, can provide a more precise and efficient treatment strategy for patients with macular edema secondary to DR and RVO. It has high clinical application value and is worthy of promotion in the comprehensive management of fundus diseases. Meanwhile, future studies should further explore individualized treatment models for patients at different etiological stages, as well as its impact on long-term recurrence rates and sustained improvement in visual function, in order to provide more reliable evidence for the systematic management of chronic fundus diseases.

Conclusion

The findings of this study indicate that conbercept combined with laser therapy offers significant advantages in improving visual acuity and retinal structure in patients with macular edema secondary to DR and RVO. This combined treatment not only significantly increased the overall treatment efficacy but also accelerated the absorption of fundus hemorrhage and

exudates, shortened the resolution time of macular edema, and promoted visual function recovery. Conbercept effectively intervenes in the pathological mechanisms by targeting VEGF and related inflammatory factors, enhancing both the depth and breadth of treatment. Additionally, the combination therapy demonstrated good safety without significant adverse reactions, highlighting its high clinical application value. However, this study has limitations including its single-center retrospective design, limited sample size, and relatively short follow-up period. Future prospective, multicenter, large-sample studies with long-term follow-up, incorporating multimodal imaging and functional assessments, are necessary to further validate the durability of conbercept's efficacy and its differential effects across various RVO types. Overall, conbercept, as an effective adjunct to laser therapy, provides a more precise and efficient treatment strategy for patients with DR- and RVO-related macular edema and is worthy of broader clinical application and further investigation.

Disclosure

The authors report no conflicts of interest in this work.

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