

Original Article

Intravitreal conbercept combined with panretinal photocoagulation improves efficacy and reduces inflammatory factors in diabetic macular edema: a retrospective study

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Abstract: Objective: To evaluate the efficacy and safety of intravitreal conbercept combined with panretinal photocoagulation (PRP) for diabetic macular edema (DME) in diabetic retinopathy (DR). Methods: This retrospective study included 160 DR patients with DME admitted from January 2022 to June 2025. Among them, 85 patients received conbercept plus PRP (the joint group) and 75 received PRP alone (the control group). Clinical efficacy, best-corrected visual acuity (BCVA, logMAR), central macular thickness (CMT), intraocular pressure (IOP), aqueous humor inflammatory factors (VEGF, IL-6, sICAM-1, bFGF), and complications were compared. Multivariate logistic regression identified independent risk factors for poor efficacy. Results: The overall effective rate was higher in the joint group (92.94% vs. 80.00%, $P=0.016$). At 6 months, the joint group showed significantly greater improvements in BCVA, CMT, and IOP (all $P<0.05$). In aqueous humor, the levels of VEGF, IL-6, sICAM-1, and bFGF decreased more significantly ($P<0.001$). The complication rate was lower (3.53% vs 12.00%, $P=0.045$). Age ≥ 65 years, diabetes duration ≥ 15 years, and the absence of conbercept treatment were independent risk factors for poor efficacy ($P<0.05$). Conclusion: Intravitreal conbercept combined with PRP effectively improves visual acuity, reduces macular edema, and lowers intraocular inflammatory factors in DR with DME, with a favorable safety profile.

Keywords: Conbercept, panretinal photocoagulation, diabetic retinopathy, macular edema, inflammatory factors

Introduction

Diabetic retinopathy (DR) is one of the most common microvascular complications of diabetes, with diabetic macular edema (DME) being the primary cause of visual impairment in patients with DR [1]. The occurrence of DME is closely related to three key factors: disruption of the blood-retinal barrier, retinal ischemia and hypoxia, and overexpression of vascular endothelial growth factor (VEGF) [2]. Currently, the first-line treatment strategies for DME include intravitreal injection of anti-VEGF drugs and laser photocoagulation therapy [3]. Panretinal photocoagulation can reduce retinal oxygen consumption and stabilize retinal structure, but it may cause worsening of macular edema or visual field defects [4]; anti-VEGF

drugs such as conbercept can rapidly reduce vascular permeability and regress macular edema, but it often requires repeated intravitreal injections, and treatment response may diminish over time in some patients [5].

Conbercept is a Class I biological drug in China, possessing fully independent intellectual property rights and obtaining an international non-proprietary name from the World Health Organization (WHO). Conbercept is a recombinant anti-VEGF fusion protein that acts as a decoy receptor. After direct intravitreal injection, it can directly bind to intravitreal VEGF, thereby reducing the content of intravitreal VEGF and inhibiting the abnormal proliferation of new capillaries [6]. A systematic review published in 2025 comprehensively elaborated on

the mechanism of action and latest research progress of conbercept, pointing out that the 2023 APAO guidelines have listed it as a recommended agent for DME treatment [7]. In recent years, multiple randomized controlled trials and real-world retrospective analyses have shown that the combination of conbercept with panretinal photocoagulation (PRP) for DME treatment is superior to PRP alone in terms of improving visual acuity, reducing macular edema, lowering the level of aqueous humor inflammatory factors, and reducing complications [8-12]. However, data on multiple inflammatory factors and macular microcirculation dynamics after combination therapy remained scarce. Therefore, this study aimed to evaluate comprehensively the efficacy, safety, and prognostic factors of conbercept combined with PRP through a retrospective analysis of clinical data from 160 patients with DR and DME.

Materials and methods

Clinical data

A retrospective analysis was conducted on the clinical data of patients diagnosed with DR accompanied by DME and treated in the ophthalmology department of Chongqing University Three Gorges Hospital from January 2022 to June 2025. A total of 160 patients were included and divided into a joint group (JG) (Conbercept combined with PRP; n=85) and a control group (CG) (PRP alone; n=75) based on their treatment regimen.

Inclusion criteria were as follows: (1) Confirmed DR accompanied by DME through fundus examination, OCT, and FFA; (2) Macular foveal thickness of the affected eye ≥ 300 μm ; (3) Age ≥ 18 years; (4) Complete clinical data and a follow-up duration ≥ 6 months.

Exclusion criteria: (1) Concurrent glaucoma, uveitis, retinal vein occlusion, and other ocular fundus diseases; (2) Had received anti-VEGF treatment or intraocular corticosteroid injection within the past 3 months [10]; (3) Previous vitrectomy or PRP treatment; (4) Severe opacity of the refractive media, making OCT examination impossible; (5) Accompanied by severe heart, liver, and kidney dysfunction.

This study was approved by the Ethics Committee of Chongqing University Three Gorges Hospital.

Treatment regime

Control group: Only panretinal photocoagulation therapy was administered. Treatment was performed using a 577 nm laser and was divided into 2-4 sessions, covering ischemic retinal areas outside the macula, including the nasal and temporal regions of the optic disc, with a 1-week interval between sessions. The spot diameter was set at 200-300 μm , the exposure time at 0.1-0.2 s, and the power at 150-300 mW until grayish-white spots appeared.

Joint group: Intravitreal conbercept injection (Chengdu Kanghong Biological Technology Co., Ltd.; National Medical Products Administration approval number: S20130012; specification: 0.5 mg/0.05 mL) was administered first. Before the surgery, the conjunctival sac was routinely disinfected and topical anesthesia was applied. The needle was vertically inserted into the sclera at a position 3.5-4.0 mm inferior-temporal to the corneal limbus, and 0.5 mg (0.05 mL) of conbercept was slowly injected. Pressure was applied to the puncture site to prevent reflux after needle withdrawal. For patients with persistent DME, injections were repeated monthly as needed.

Main indicators

(1) Clinical efficacy: Evaluated according to the "Diagnostic and Therapeutic Effect Evaluation Criteria for Clinical Diseases". Excellent efficacy was defined as an improvement in best-corrected visual acuity (BCVA) of ≥ 2 lines (a logMAR reduction ≥ 0.2) and a CMT decrease of $\geq 20\%$. Effective was defined as an improvement in BCVA of ≥ 1 line (logMAR reduction ≥ 0.1) and a CMT decrease of $\geq 10\%$ but $< 20\%$. Ineffective was defined as failure to meet the above criteria. The overall response rate (ORR) = (excellent cases + effective cases) / total cases $\times 100\%$.

(2) Visual acuity changes: Before treatment and 6 months after treatment, BCVA was measured using the international standard logarithmic visual acuity chart (converted to logMAR notation).

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Table 1. Comparison of baseline characteristics between the two groups

Factor	Joint Group n=85	Control Group n=75	χ^2	P
Sex			0.002	0.960
Male	45 (52.94)	40 (53.33)		
Female	40 (47.06)	35 (46.67)		
Age (years)			0.009	0.926
≤65	30 (35.29)	27 (36.00)		
>65	55 (64.71)	48 (64.00)		
BMI (kg/m ²)			0.245	0.620
≤23	42 (49.41)	40 (53.33)		
>23	43 (50.59)	35 (46.67)		
History of smoking			0.017	0.896
Yes	49 (57.65)	44 (58.67)		
No	36 (42.35)	31 (41.33)		
Diabetes duration			0.036	0.849
≤15 years	50 (58.82)	43 (57.33)		
>15 years	35 (41.18)	32 (42.67)		
Affected eye			0.006	0.937
Left eye	47 (55.29)	41 (54.67)		
Right eye	38 (44.71)	34 (45.33)		

(3) Foveal thickness: The foveal thickness (CMT, μ m) was measured before and 6 months after treatment using frequency-domain OCT.

(4) Intraocular pressure: The intraocular pressure (IOP, mmHg) was measured before and 6 months after treatment using a non-contact tonometer.

Secondary indicators

(1) Intraocular fluid inflammatory factors: Aqueous humor samples were collected before and 3 months after treatment. The levels of VEGF, interleukin-6 (IL-6), soluble intercellular adhesion molecule-1 (sICAM-1), and basic fibroblast growth factor (bFGF) were measured using ELISA.

(2) Complications and safety: The occurrence of complications within 6 months after treatment was recorded, including vitreous hemorrhage, intraocular pressure (IOP) >21 mmHg and an increase of $\geq$ 5 mmHg from baseline, persistent macular edema (CMT still $\geq$ 300 μ m at 3 months after treatment), endophthalmitis, retinal detachment, etc. Additionally, the number of additional PRP treatments was recorded during the entire follow-up period.

(3) Blood flow density in the macular region: OCTA was used to measure the blood flow density of the superficial capillary plexus (SCP, %) and the deep capillary plexus (DCP, %) before and 6 months after treatment.

(4) Factors affecting efficacy: Data on patient age, gender, duration of diabetes, HbA1c, baseline BCVA, baseline CMT, history of hypertension, baseline VEGF, and inflammatory factor levels were collected for univariate and multivariate logistic regression analysis (with "poor efficacy" or ineffective as the dependent variable).

Statistical methods

SPSS 27.0 software was applied for data analysis. Measured data were expressed as mean $\pm$ standard deviation. Pairwise t-tests and independent sample t-tests were used for intra-group comparisons before and after treatment and inter-group comparisons, respectively. Enumerated data were expressed as number of cases (percentage), and χ^2 tests were adopted for inter-group comparisons. Logistic regression analysis was utilized for independent factors analysis. $P < 0.05$ was considered significant.

Results

General data

The JG and CG were comparable in terms of BMI, sex, age, duration of diabetes, history of hypertension, and other characteristics ($P > 0.05$; **Table 1**).

Comparison of treatment efficacy

After treatment, the JG achieved an evidently higher ORR than the CG (92.94% [79/85] vs. 80.00% [60/75], $\chi^2=5.852$, $P=0.016$; **Table 2**).

Comparison of visual acuity changes and foveal thickness

Before treatment, the BCVA (logMAR) and CMT between the two groups were similar ($P > 0.05$). After treatment, both parameters improved notably in both groups ($P < 0.05$), and the JG

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Table 2. Comparison of treatment efficacy between the two groups

Therapeutic Effect	Joint Group n=85	Control Group n=75	χ^2	P
Markedly Effective	46 (54.12)	30 (40.00)	-	-
Effective	33 (38.82)	30 (40.00)	-	-
Ineffective	6 (7.06)	15 (20.00)	-	-
Overall Response Rate	79 (92.94)	60 (80.00)	5.852	0.016

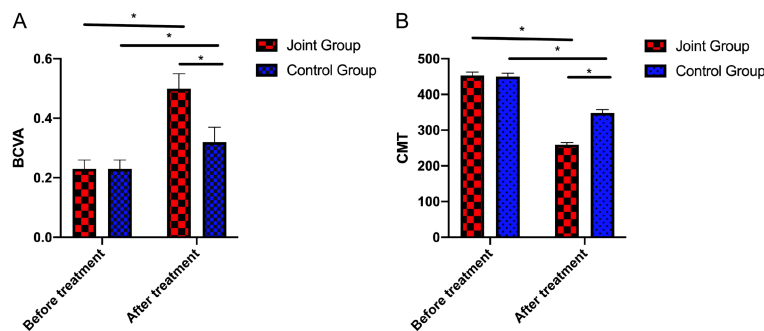


Figure 1. Comparison of visual acuity changes and macular foveal thickness between the groups. A. BCVA; B. CMT. Notes: BCVA, best-corrected visual acuity; CMT, central macular thickness; *P<0.05.

Table 3. Comparison of intraocular pressure changes between the two groups

Time	Joint Group n=85	Control Group n=75	t	P
Before Treatment	35.63±1.08*	35.7±1.1*	0.464	0.644
After Treatment	22.4±1.06	25.67±1.13	18.88	<0.001

Note: *P<0.05, compared to after treatment values.

showed a more pronounced improvement than the CG (P<0.001; **Figure 1**).

Comparison of intraocular pressure changes

Before treatment, the IOP difference was insignificant between the two groups (P>0.05). Six months after treatment, IOP in both groups decreased evidently (P<0.05), and such decline in the JG was lower than in the CG (P<0.001; **Table 3**).

Comparison of inflammatory factors in aqueous humor

Baseline aqueous humor inflammatory factors were comparable between the two groups (P>0.05). At 3 months after treatment, VEGF, IL-6, sICAM-1, and bFGF levels in the JG were markedly lower than those in the CG (P<0.001; **Figure 2**).

Comparison of complications and adverse events

The overall incidence of complications of JG was substantially lower than that in the CG (3.53% [3/85] vs. 12.00% [9/75], $\chi^2=4.029$, P=0.045). The JG only reported 1 case each of vitreous hemorrhage, elevated intraocular pressure, and persistent macular edema, whereas the corresponding numbers in the CG were 4, 2, and 3. Neither group experienced endophthalmitis or retinal detachment (**Table 4**).

Multivariate logistic regression analysis affecting treatment efficacy

Taking poor efficacy (ineffective) as the dependent variable, factors such as age, gender, duration of diabetes, and treatment regimen were included for multivariable logistic regression analysis. The results showed that age ≥ 65 years, duration of diabetes ≥ 15 years, and no combination with conbercept treatment were independent risk factors for poor efficacy (**Tables 5-7**).

Discussion

This retrospective study suggested that the combining intravitreal conbercept injection with PRP for DR and DME was significantly superior to PRP alone in terms of overall clinical efficacy, visual function recovery, macular edema regression, inflammatory factor regulation, complication control, and macular blood flow perfusion. These results support the clinical benefit of combined therapy and offer additional data for practice.

Firstly, in terms of symptom improvement, JG patients exhibited notably better visual function, intraocular pressure, and regression of macular edema compared to those in the CG. This may be attributed to complementary

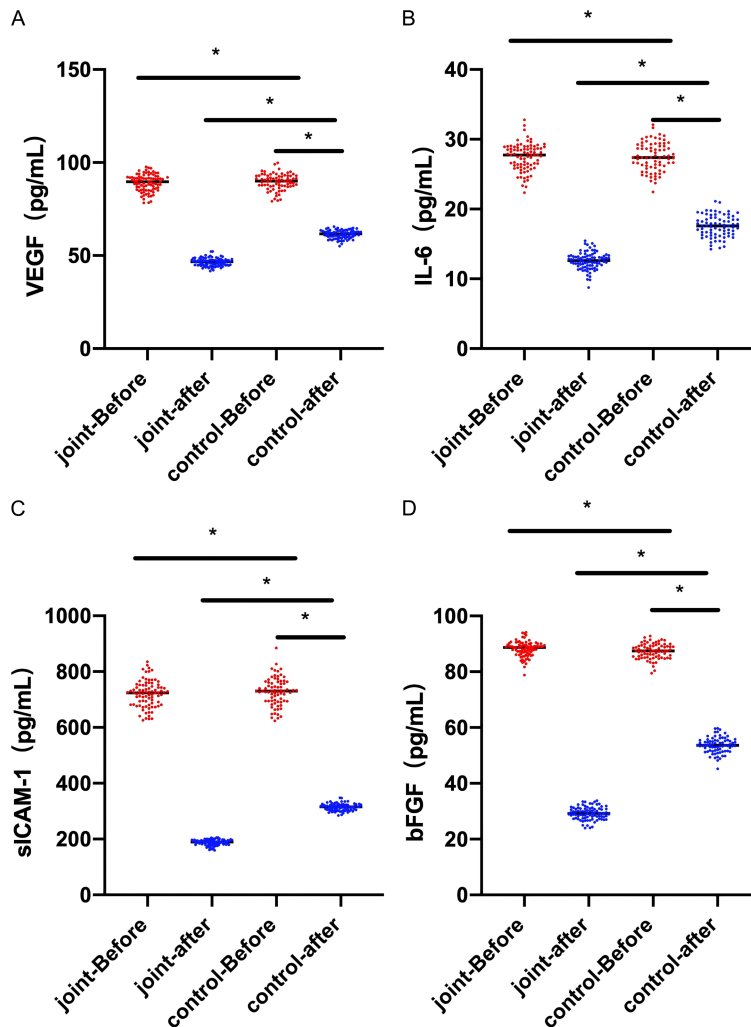


Figure 2. Comparison of aqueous humor inflammatory factors between the two groups of patients before and after treatment. A. VEGF; B. IL-6; C. sICAM-1; D. bFGF. Notes: VEGF, vascular endothelial growth factor; IL-6, interleukin-6; sICAM-1, soluble intercellular adhesion molecule-1; bFGF, basic fibroblast growth factor; *P<0.05.

Table 4. Comparison of complications and adverse events between the two groups

Adverse Reaction	Joint Group (n=85)	Control Group (n=75)	χ^2	P
Vitreous hemorrhage	1 (1.18)	4 (5.33)	-	-
Elevated intraocular pressure	1 (1.18)	2 (2.67)	-	-
Persistent macular edema	1 (1.18)	3 (4.00)	-	-
Endophthalmitis	0 (0)	0 (0)	-	-
Retinal detachment	0 (0)	0 (0)	-	-
Overall incidence rate	3 (3.53)	9 (12.00)	4.029	0.045

mechanisms of the two therapies: first, conbercept, as a multi-target anti-VEGF drug, can

DR patients with DME who require rapid control of macular edema and have high-risk factors,

simultaneously inhibit VEGF-A, VEGF-B, and PlGF, rapidly reducing vascular permeability and thereby quickly alleviating macular leakage, creating a more stable retinal microenvironment for subsequent laser treatment [5, 6]. Second, PRP inhibits the continuous production of VEGF upstream by destroying peripheral ischemic retina and reducing total retinal oxygen consumption [4]. Mechanistically, anti-VEGF therapy provides rapid action by directly targeting existing vascular leakage, whereas laser therapy offers sustained benefits by addressing the underlying ischemic drivers. However, the exact molecular interplay requires further study [9-11]. Multi-center randomized controlled trials have shown that conbercept, whether administered in a 3+PRN or 6+PRN loading regimen, significantly improved BCVA and CMT, with the initial 6-injection treatment group showing a trend toward superior efficacy [14]. For patients with DME of different optical coherence tomography (OCT) types, studies have found that conbercept reduces CMT the most in three OCT patterns: diffuse retinal thickening, cystoid macular edema, and serous retinal detachment [10]. For high-risk proliferative DR patients, studies have confirmed that PRP combined with conbercept not only promotes neovascular regression more effectively but also greatly reduces the need for subsequent vitreous surgery [12]. The above evidence collectively suggests that for

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Table 5. Univariate analysis of factors associated with treatment efficacy

Variable	Effective Group (n=139)	Ineffective Group (n=21)	χ^2	P
Sex			0.005	0.942
Male (n=85)	74 (53.24)	11 (52.38)		
Female (n=75)	65 (46.76)	10 (47.62)		
Age			4.885	0.027
>65 (n=57)	87 (62.59)	16 (76.19)		
≤65 (n=103)	52 (37.41)	5 (23.81)		
BMI (kg /m ²)			0.012	0.911
>23 (n=78)	68 (48.92)	10 (47.62)		
≤23 (n=82)	71 (51.08)	11 (52.38)		
History of smoking			0.010	0.922
Yes (n=93)	81 (58.27)	12 (57.14)		
No (n=67)	58 (41.73)	9 (42.86)		
Diabetes Duration			19.09	<0.001
>15 years (n=67)	49 (35.25)	18 (85.71)		
≤15 years (n=93)	90 (64.75)	3 (14.29)		
Treatment Regime			5.825	0.016
With conbercept (n=85)	79 (56.83)	6 (28.57)		
Without conbercept (n=75)	60 (43.17)	15 (71.43)		

Table 6. Assignment of variables

Variable	Coding
Diabetes Duration	>15 years = 1, ≤15 years = 0
Age	>65=1, ≤65=0
Treatment Regime	Without conbercept = 1, With conbercept = 0

Table 7. Multivariable analysis of independent risk factors for poor treatment efficacy

Variable	B	S.E	Wald	P	OR	95% CI	
						Lower limit	Upper limit
Diabetes Duration	-1.689	0.677	6.232	0.013	0.185	0.049	1.696
Age	-2.109	0.557	14.312	0.001	0.121	0.041	1.362
Treatment Regime	1.029	0.501	4.219	0.040	0.615	1.048	7.475

early combination therapy with conbercept can yield greater benefit [19].

DME is essentially characterized by a combination of inflammation and vascular leakage. Although anti-VEGF therapy alone can inhibit VEGF, other inflammatory factors such as IL-6, sICAM-1, and bFGF also contribute to the disruption and continuous leakage of the blood-retinal barrier [2, 16]. This study shows that the reduction in multiple inflammatory factors in the aqueous humor was more pronounced in the JG, indicating that combined treatment has a more comprehensive anti-inflammatory effect, which is consistent with recently pub-

lished real-world research results [11]. A prospective study in elderly patients with DME found that eyes with higher baseline aqueous humor VEGF and IL-6 levels often achieved greater anatomic improvements after treatment with conbercept. These biomarkers show promise for incorporation into multifactorial prediction models to guide individualized treatment [11]. Another study confirmed that VEGF-A and several inflammatory mediators, including IL-6 and IL-8, declined notably after intravitreal anti-VEGF treatment in DME patients [20, 21]. In addition, sICAM-1 is a key mediator of blood-retinal barrier disruption, and its decreased level reflects the repair of

barrier function; bFGF is involved in neovascularization and fibrous proliferation, and its downregulation helps to inhibit the progression of fibrosis in the late stage of the disease [5, 22]. The decrease of multiple inflammatory factors was greater after conbercept combined with PRP, which may suggest that the two treatments synergistically inhibited the retinal inflammatory vascular leakage process, but the specific molecular mechanisms require further investigation. Furthermore, this study only measured four protein factors in the aqueous humor. The biological changes observed cannot be directly equivalent to the activation or blockade of signaling pathways. In the future, it needs to be verified by cell or animal experiments. In recent years, multiple researches have been exploring precision treatment strategies based on aqueous humor biomarkers to achieve individualized optimization of anti-VEGF therapy for DME patients. Furthermore, maintaining blood flow density in the macular region is crucial for long-term visual function protection, and OCTA, as a noninvasive, layer-specific, and quantitative imaging tool, can accurately assess the microvascular structure and avascular area in the macular region [13, 17, 18, 23]. In this study, the blood flow density of the deep capillary plexus in the JG was significantly higher than that of the CG, suggesting that combination therapy may be more effective in protecting the microvascular structure of the inner retina. A longitudinal study using OCTA to dynamically evaluate changes in microvascular parameters after treatment in PDR patients confirmed for the first time that quantitative OCTA parameters can effectively reflect ocular microvascular response after treatment with conbercept [15]. Another clinical study using OCTA also demonstrated that conbercept treatment can quantitatively improve the macular avascular zone area and capillary density in DME patients, providing a new technology for precise microvascular assessment for DME [17]. In addition, some studies have constructed an OAGB staging system based on OCTA parameters to assess the severity of DR, providing a new reference paradigm for enrollment selection and prognostic assessment in combination therapy [24].

In terms of safety, the JG had a markedly lower overall incidence of complications than the CG. Multi-center studies have shown that patients'

core quality of life (as measured by the NEI-VFQ-25 score) evidently improves after treatment with conbercept combined with PRP, further supporting the comprehensive value of this regimen in terms of functional gains and life quality enhancement [25]. The lower complication rates observed in the combined group may be associated with reduced neovascular activity and a decreased requirement for intense laser treatment. Several mechanisms may contribute to this finding. First, the combined therapy may alleviate laser-induced inflammatory responses and reduce exacerbation of macular edema; Second, suppression of neovascular activity may decrease the risk of intraoperative and postoperative hemorrhage; Third, improvement in retinal ischemia may reduce the necessity for subsequent laser retreatment. Finally, the multi-factor regression analysis in this study confirmed that advanced age (≥ 65 years), long disease duration (≥ 15 years), and the absence of conbercept treatment were three independent risk factors for poor efficacy. Multi-center studies have also found that advanced age is one of the important factors closely related to the outcomes of conbercept treatment [14]. In addition, some studies have reported that patients with preoperative comorbidities such as renal insufficiency and proliferative membranes may have a reduced response to anti-VEGF therapy, with a slower regression rate of DME, requiring more intensive initial treatment. These findings further enrich the selection criteria for the indications of combination therapy [26]. Based on the above risk factors, it is recommended that patients with two or more risk factors receive combination therapy earlier and more aggressively in clinical practice. A more intensive anti-VEGF loading regimen should be adopted in the initial stage, together with stricter glycemic control and more frequent follow-up [27, 28].

In the present study, intravitreal conbercept combined with PRP provided better control of macular edema, improved visual acuity, reduced intraocular inflammatory factor levels, and demonstrated good safety in DR patients complicated by DME. Independent factors affecting treatment efficacy included age, duration of diabetes, level of blood glucose control, and whether conbercept is used in combination. This combined approach is wor-

thy of application in DR patients accompanied by DME. However, this study was a retrospective single-center analysis, which is subject to selection bias and a limited sample size. Additionally, the study was not blinded. The follow-up period was only 6 months, lacking long-term efficacy and safety data for more than one year. Although evident down-regulation of aqueous humor inflammatory factors was observed, dynamic detection at multiple time points was not conducted, making it difficult to establish the correlation between their temporal changes and disease recurrence. In addition, beyond the indicators already covered in this study, there are still many key clinical issues remaining to be explored, including the optimal timing of laser treatment, the potential benefit of combining with steroid therapy, and the efficacy in patients at different DR stages. This study detected only VEGF, IL-6, sICAM-1 and bFGF, which failed to reflect comprehensively the complex inflammation-angiogenesis network in aqueous humor. Prospective studies in the future can expand the sample size and systematically screen novel markers related to response to combination therapy by using multiplex immunoassay or proteomics technology. Future studies could also establish diabetic animal models, combined with fluorescence angiography and molecular biology technology, to explore the effect of combined treatment on the ultrastructure of the blood retinal barrier.

Disclosure of conflict of interest

None.

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