

## Retrospective Study

**Conbercept combined with laser photocoagulation in the treatment of diabetic macular edema and its influence on intraocular cytokines**

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**Specialty type:** Ophthalmology**Provenance and peer review:**

Unsolicited article; Externally peer reviewed.

**Peer-review model:** Single blind**Peer-review report's scientific quality classification**Grade A (Excellent): 0  
Grade B (Very good): B, B  
Grade C (Good): C  
Grade D (Fair): 0  
Grade E (Poor): 0**P-Reviewer:** Strain WD, United Kingdom; Unnikrishnan R, India; Horowitz M, Australia**Received:** May 31, 2023**Peer-review started:** May 31, 2023**First decision:** June 14, 2023**Revised:** June 19, 2023**Accepted:** July 14, 2023**Article in press:** July 14, 2023**Published online:** August 15, 2023

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The prevalence of diabetes mellitus (DM) in China is high, and the base is broad. Diabetic retinopathy (DR) is a critical condition affecting the life and health of a nation and its economic development. DR is a common complication of DM.

**AIM**

To investigate the efficacy of laser photocoagulation combined with intravitreal injection of conbercept for treating macular edema.

**METHODS**

Overall, 130 patients with diabetic macular edema (DME) hospitalized in The Third People's Hospital of Changzhou from January 2019 to June 2022 were retrospectively included. According to the treatment plan, 130 patients with DME were categorized into an observation and a control group, with 65 patients in each group. The control group received laser photocoagulation, and the observation group received laser photocoagulation with intravitreal injection of conbercept. Observe changes in vision, cytokines in the eye and so on.

**RESULTS**

The total efficacy rate in the observation group (93.85%) was higher than that in the control group (78.46%) ( $P < 0.05$ ). In both groups, the best corrected visual acuity correction effect improved after treatment, and the observation group was superior to the control group ( $P < 0.05$ ). Retinal thickness and central macular thickness improved after treatment, and the observation group was superior to the control group ( $P < 0.05$ ). The levels of vascular endothelial growth factor, interleukin-6, soluble intercellular adhesion molecule-1, and basic fibroblast growth factor in both groups improved after treatment, and the observation group was superior to the control group ( $P < 0.05$ ).

**CONCLUSION**

In patients with macular edema, combining laser photocoagulation and intravitreal injections of conbercept for DME is a more effective and safer strategy to improve vision, and lower intraocular cytokine levels.

**Key Words:** Conbercept; Laser photocoagulation; Diabetes treatment; Diabetic retinopathy; Diabetic macular edema; Intraocular cytokines

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**Core Tip:** This study investigated the efficacy of intravitreal injection of conbercept combined with retinal laser photocoagulation in treating diabetic retinopathy (DR) with macular edema and compared the effectiveness of conbercept injection based on laser photocoagulation in the treatment of DR. It also provides a new scheme for clinical treatment of DR with macular edema. The results showed that intravitreal injection of conbercept combined with laser photocoagulation could be more effective in treating diabetic macular edema, shortening the treatment process, and reducing the level of cytokines in the eye. Thus, this treatment plan warrants further promotion.

**Citation:** Zhan HQ, Zhou JL, Zhang J, Wu D, Gu CY. Conbercept combined with laser photocoagulation in the treatment of diabetic macular edema and its influence on intraocular cytokines. *World J Diabetes* 2023; 14(8): 1271-1279

**URL:** <https://www.wjgnet.com/1948-9358/full/v14/i8/1271.htm>

**DOI:** <https://dx.doi.org/10.4239/wjd.v14.i8.1271>

## INTRODUCTION

Diabetic retinopathy (DR) is a common complication in patients with diabetes. DR is a critical factor affecting people's lives, health, and economic development. Furthermore, there are many reasons for vision loss in patients with DR, including diabetic macular edema (DME). However, the etiology of DME is unknown and may be related to reduced retinal barrier function in macular DME, which mainly appears as a retinal thickening and can cause patients to develop significant DME, primarily manifesting as a retinal thickening and can cause patients to develop substantial visual impairment, which requires active treatment[1]. Historically, the main clinical treatment strategy for DME has been laser photocoagulation of the retina under glycemic control, where laser energy causes protein denaturation and coagulation, capillary and outer retinal wall occlusion, and reduced macular blood flow[2]. Laser photocoagulation is important in treating retinal vascular diseases and cannot be completely replaced by various intraocular drugs. The predominant technique in the clinical treatment of DR is laser photocoagulation because it inhibits intraocular vascular growth, reduces macular edema, and improves visual acuity[3].

DR is primarily caused by metabolic abnormalities and organ dysfunction due to diabetes. Therefore, laser photocoagulation alone improves symptoms and effectively prevents DR[4]. As research progresses, it is currently known that the development of DME is closely related to vascular endothelial growth factor [hereafter referred to as vascular endothelial growth factor (VEGF)]. Intravitreal administration of anti-VEGF drugs can rapidly improve DME symptoms and has attracted significant clinical attention. Conbercept is a humanized anti-VEGF drug manufactured domestically and with a strong presence in the domestic market, available for treating ocular vascular diseases with remarkable results[5]. This study aimed to evaluate the combined effects of conbercept intravitreal administration and laser retinal photocoagulation for DME, compare the effects of combined treatment and laser photocoagulation alone, and propose a new clinical treatment system for DME in DR.

## MATERIALS AND METHODS

### General information

Overall, 130 patients with DME who were hospitalized in The Third People's Hospital of Changzhou between January 2019 and June 2022 were retrospectively included. According to the treatment plan, 130 patients with DME were categorized into an observation and a control group, with 65 patients in each group. The observation group comprised 39 males (39 diseased eyes) and 26 females (26 diseased eyes). The age of the patients in this group was 33-79 (51.07 ± 12.50) years. The disease duration in the selected patients ranged from 1 to 4 (2.49 ± 0.34) wk. The control group comprised 36 males (48 diseased eyes) and 29 females (39 diseased eyes). The age of the patients in the control group ranged from 34 to 78 (52.48 ± 11.37) years. Their disease duration ranged from 1 to 4 (2.58 ± 0.37) wk. No significant differences were found in the general characteristics (sex, age, or disease duration) between the two groups ( $P > 0.05$ ).

### Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) Age  $\geq 18$ , met diagnostic criteria for DR; (2) met DME diagnostic standards, best corrected visual acuity (BCVA)  $< 0.6$ , and central macular thickness (CMT)  $\geq 250$   $\mu\text{m}$ ; and (3) no severe organ

dysfunction, such as heart, liver, and kidney.

The exclusion criteria were as follows: (1) Previous cataract or other eye surgeries; (2) other types of maculopathy; and (3) patients who could not undergo eye surgery[6].

### **Therapeutic method**

Intravitreal injection of conbercept and laser photocoagulation treatment were used in the observation group; antibiotic eye drops were routinely used 5 d preoperatively. Intravitreal injections of conbercept included disinfection of a drape, topical anesthesia, eyelid opener, povidone-iodine solution (5%), conjunctival sac disinfection, and normal saline irrigation. A 1-mL disposable syringe was connected to a 30 G needle to suction 0.05 mL conbercept injection. The tip of the needle was perpendicular to the eyeball wall, and the needle was inserted approximately 1 cm from the flat part of the ciliary body 3.5-3.8 mm behind the superior temporal limbus.

The needle was confirmed to reach the vitreous cavity from the pupil area, slowly push the injection, pull it out after completion, and gently press the needle eye with a cotton swab for 2 min. Tobramycin and Dexamethasone Eye Ointment were applied to the conjunctival sac, a bandage was used, and antibiotics were administered for 3 d[7].

The 532 nm laser pan-retinal photocoagulation: 1 wk after intravitreal injection of conbercept, laser system (California, Lumenis, United States), wavelength 532 nm, spot diameter 200-300  $\mu$ m, exposure time 0.2-0.3 s, power level I-III, and Spaced one spot diameter apart. First, photocoagulation of the uncovered part of the vitreous hemorrhage was performed 3-4 times at 1-wk intervals as the accumulated blood was absorbed. The total effective photocoagulation volume was 1200-1500 points. It was completed by senior doctors of the same specialty[8].

The control group was treated with 532 nm laser photocoagulation, and the procedure was the same as that of the observation group.

### **Detection methods of related indicators**

(1) BCVA was measured according to the international standard eye chart; (2) retinal thickness was measured using optical coherence tomography (OCT, Heidelberg, Germany); (3) CMT was measured using OCT; (4) a 5-mL was collected in the morning in a common vacuum tube and centrifuged at 3500 rpm for 15 min at a centrifuge radius of 8 cm. The upper serum was collected, and the level of VEGF was measured using ELISA; (5) vitreous fluid from patients was collected and diluted, and interleukin-6 (IL-6) expression and soluble intercellular adhesion molecule-1 (sICAM-1) and basic fibroblast growth factor (BFGF) levels were measured using ELISA; and (6) the adverse reactions during treatment were recorded in both groups[9].

### **The criterion of therapeutical effect**

Significant effect: Fundus fluorescein angiography showed retinal capillaries, arteriolar non-perfusion area, and no neovascularization and visual acuity reached 5.0 or improved more than 2 lines; effective: Retinal capillaries, arteriolar non-perfusion area, and neovascularization significantly reduced, visual acuity improved 1 line; ineffective: retinal capillaries, arteriolar non-perfusion area, and neovascularization did not decrease or aggravate, and visual acuity did not improve. Ametropia refers to corrected visual acuity. Total effective rate = (effective + markedly effective)/total cases  $\times$  100%[10].

### **Observation target**

(1) The BCVA was measured using an international standard visual acuity chart at four-time points: Before treatment, 1 mo after treatment, 3 mo after treatment, and 6 mo after treatment; (2) the retinal thickness was measured using an OCT scanner at four-time points: Before treatment, 1 mo after treatment, 3 mo after treatment, and 6 mo after treatment; (3) CMT was measured using OCT before treatment, 1 mo of treatment, 3 mo of treatment, and 6 mo after treatment; (4) cytokine levels: before treatment, after 1 mo of treatment, after 3 mo of treatment, and after 6 mo of treatment, 0.2 mL of vitreous fluid was collected from the patient, diluted, and assayed using enzyme-linked immunoassay for VEGF and IL-6 and sICAM-1 and BFGF[11]. Adverse events also need to be recorded: The occurrence of adverse reactions during treatment in both groups, such as elevated intraocular pressure, endophthalmitis, vitreous hemorrhage, and retinal detachment, among others[12].

### **Statistical analysis**

The clinical data were analyzed using SPSS statistical software. The test data followed a normal distribution and were expressed as mean  $\pm$  SD regarding homogeneity of variance and compared using independent sample *t*-tests. Count data were expressed as *n* (%) using the  $\chi^2$  test; statistical significance was set at  $P < 0.05$ .

## **RESULTS**

### **Clinical effects**

The patients in both groups showed high efficacy; however, the total efficacy rate in the observation group was higher than that in the control group ( $P < 0.05$ ) (Table 1).

### **Comparison of two groups of BCVA**

The BCVA of the control and observation groups before treatment was not significantly different ( $P > 0.05$ ). After 1 mo of

**Table 1 Clinical effects**

Group	Number of cases	Invalid, n (%)	Valid, n (%)	Excellent, n (%)	Total effective rate (%)
Control group	65	14 (21.54)	41 (63.08)	10 (15.38)	78.46
Observation group	65	4 (6.15)	41 (63.08)	20 (30.77)	93.85
$\chi^2$ value					8.88
<i>P</i> value					0.04

treatment, the BCVA in both groups improved. After 3 mo and 6 mo of treatment, the BCVA in both groups improved significantly, and that in the observation group was superior to that in the control group. According to the independent samples *t*-test, the changes in BCVA in the two groups were statistically different at the three-time points after treatment and were comparable ( $P < 0.05$ ), as shown in [Table 2](#).

### Retinal thickness

No significant difference was observed in the retinal thickness between the two groups before treatment ( $P > 0.05$ ). After 1 mo of treatment, it was visually evident from the images that the retinal thickness of both groups improved. Retinal thickness in both groups improved significantly after 3 and 6 mo of treatment, and the effect in the observation group was better than that in the control group. According to the *t*-test, a significant variation existed in retinal thickness changes between the two groups at the three time points after treatment ( $P < 0.05$ ) ([Table 3](#)).

### Comparison of CMT between two groups of patients

The difference in CMT between the two groups before treatment was not statistically significant ( $P > 0.05$ ). The CMT in both groups improved after 1 mo of treatment. The CMT in both groups could be found to be substantially improved after 3 mo and 6 mo of treatment, and the effect of the observation group was better than that of the control group. Notably, the changes in CMT in both groups at the two-time points were statistically different ( $P < 0.05$ ) ([Table 4](#)).

### Cytokine levels

The data showed no statistical discrepancy in the levels of VEGF, IL-6, sICAM-1, and BFGF between the observation control group before treatment ( $P > 0.05$ ). The cytokine levels in both groups gradually decreased after 1 mo, 3 mo, and 6 mo of treatment. According to the independent samples *t*-test, VEGF, IL-6, sICAM-1, and BFGF levels were statistically different between the observation and control groups at the three time points after treatment ( $P < 0.05$ ), as shown in [Tables 5-8](#).

### Untoward effect

The two groups had 2 and 3 cases of intraocular pressure hypertension and 1 and 1 case of vitreous injection site hemorrhage, respectively. Retinal detachment or fundus lesions were not observed in either group. The total incidence of adverse events in the control and observation groups was 4.61% and 6.15% (control and observation), respectively, and no significant difference was found between the two groups in the total incidence of adverse events. ( $\chi^2 = 2.222$ ,  $P > 0.05$ ).

## DISCUSSION

Studies have demonstrated that approximately 6.8% of patients with diabetes experience vision loss due to DME. Clinically, DME is defined as a retinal thickening or hard exudation within 1.5 mm of the fovea. The mechanism of DME may involve a local inflammatory reaction or oxidative stress reaction[13]. It damages the retinal barrier and increases retinal permeability. Some proteins and water molecules enter the parenchymal layer from outside the retina, increasing intercellular space[14]. If these components converge into the macular area, they will cause retinal thickening and visual impairment in the macular area[15]. Intravitreal injection of anti-VEGF drugs and laser photocoagulation are options for treating DME; however, both methods have limitations. Photocoagulation has a long history of use in treating DR. Photocoagulation can inhibit blood vessel proliferation, relieve hypoxia in the inner retina, and improve visual function. Patients with DR still experience vision loss shortly after simple photocoagulation treatment, which is related to the failure to eliminate the underlying cause of DR formation. Abnormal angiogenesis plays a key role in the occurrence and development of DR. Retinal laser photocoagulation is used to transform laser energy into heat energy and then use its consistency and strong directionality to form scars at specific locations in the retina to repair eye tissue[16]. However, it has the risk of burning the retinal fovea and damaging the retinal pigment epithelial cells, and the treatment effect in moderate to severe DME is not ideal[17]. Anti-VEGF drugs reduce angiogenesis by inhibiting the binding of VEGF to its receptors[18]. Some patients do not respond to anti-VEGF drugs. Although anti-VEGF drugs can improve the visual acuity and anatomical structure in patients with DME, they cannot replace retinal laser photocoagulation. Therefore, laser photocoagulation in combination with the injection of an anti-VEGF is recommended. Conbercept, which is a fusion protein extracted from hamster ovarian cells, has antiangiogenic and antiproliferative effects on endothelial cells. It has been successfully used to treat wet age-related macular degeneration[19]. Therefore, this study used a combination

**Table 2 Comparison of best-corrected visual acuity before and after treatment**

Group	Number of cases	BCVA			
		Prior treatment	One month of treatment	Three months of treatment	Treatment for 6 mo
Control group	65	0.07 ± 0.02	0.22 ± 0.08 <sup>1</sup>	0.30 ± 0.16 <sup>1,2</sup>	0.49 ± 0.20 <sup>1,2,3</sup>
Observation group	65	0.07 ± 0.02	0.21 ± 0.06 <sup>1</sup>	0.44 ± 0.16 <sup>1,2</sup>	0.62 ± 0.22 <sup>1,2,3</sup>
<i>t</i> value		1.224	-5.221	-6.804	-4.439
<i>P</i> value		0.223	< 0.001	< 0.001	< 0.001

<sup>1</sup>Indicates the intra-group comparison with that before treatment, *P* < 0.05.

<sup>2</sup>Indicates that compared with 1 mo after treatment, *P* < 0.05.

<sup>3</sup>Indicates <sup>a</sup>*P* < 0.05, in the group compared with 3 mo of treatment.

BCVA: Best-corrected visual acuity.

**Table 3 Retinal thickness before and after treatment**

Group	Number of cases	Retinal thickness (μm)			
		Prior treatment	One month of treatment	Three months of treatment	Treatment for 6 mo
Control group	65	637.20 ± 101.96	431.12 ± 90.22 <sup>1</sup>	320.16 ± 88.71 <sup>1,2</sup>	241.92 ± 70.43 <sup>1,2,3</sup>
Observation group	65	638.39 ± 103.16	316.31 ± 86.72 <sup>1</sup>	221.43 ± 90.22 <sup>1,2</sup>	170.62 ± 72.34 <sup>1,2,3</sup>
<i>t</i> value		-0.492	6.216	6.535	5.863
<i>P</i> value		0.624	< 0.001	< 0.001	< 0.001

<sup>1</sup>Indicates the intra-group comparison with that before treatment, *P* < 0.05.

<sup>2</sup>demonstrates that compared with 1 mo after treatment, *P* < 0.05.

<sup>3</sup>Indicates *P* < 0.05, in the group compared with 3 mo of treatment.

**Table 4 Before and after central macular thickness treatment**

Group	Number of cases	CMT (μm)			
		Prior treatment	One month of treatment	Three months of treatment	Treatment for 6 mo
Control group	65	360.60 ± 41.62	307.32 ± 39.42 <sup>1</sup>	270.38 ± 34.67 <sup>1,2</sup>	236.71 ± 32.31 <sup>1,2,3</sup>
Observation group	65	357.63 ± 42.51	249.31 ± 36.21 <sup>1</sup>	221.62 ± 31.62 <sup>1,2</sup>	183.26 ± 33.32 <sup>1,2,3</sup>
<i>t</i> value		0.493	8.949	8.611	9.175
<i>P</i> value		0.623	< 0.001	< 0.001	< 0.001

<sup>1</sup>Indicates the intra-group comparison with that before treatment, *P* < 0.05.

<sup>2</sup>Indicates that compared with 1 mo after treatment, *P* < 0.05.

<sup>3</sup>Indicates intra-group comparison with 3-mo treatment, *P* < 0.05.

CMT: Central macular thickness.

treatment protocol for DME and examined its efficacy and safety to explore a more economical and effective treatment scheme for DME[20].

Analysis of the data before and after the four treatment periods revealed that laser photocoagulation combined with conbercept injection had a better treatment effect on DME, which can effectively improve the visual quality of patients and inhibit retinal thickening[21]. Retinal laser photocoagulation reduces macular edema in the following two ways: One is by blocking the capillary network through the thermal effect of the laser, which decreases the permeability of the retina and reduces the infiltration rate; and other is in the retinal epithelium that damages the photoreceptor cells in the retina and decreases their VEGF expression, which decreases angiogenesis in the retina and improves its hypoxic state. This has proven to be a practical and effective treatment method; however, its treatment time is considerably long and can cause visual field defects, thereby reducing its effectiveness[22]. In combination with retinal laser photocoagulation, DME can be treated from the following two perspectives: inhibition of macular effusion and multitargeted inhibition of VEGF expression. In our study, we found that compazepib significantly increased laser penetration during retinal laser photocoagulation and enhanced its efficacy[23].

**Table 5 Levels of vascular endothelial growth factor before and after treatment**

Group	Number of cases	VEGF (ng/mL)			
		Prior treatment	One month of treatment	Three months of treatment	Treatment for 6 mo
Control group	65	423.73 ± 76.35	336.73 ± 65.28 <sup>1</sup>	170.30 ± 41.32 <sup>1,2</sup>	106.32 ± 10.71 <sup>1,2,3</sup>
Observation group	65	424.32 ± 77.31	301.62 ± 63.78 <sup>1</sup>	110.32 ± 36.72 <sup>1,2</sup>	66.79 ± 10.21 <sup>1,2,3</sup>
<i>t</i> value		-0.151	3.512	8.707	21.818
<i>P</i> value		0.880	< 0.001	< 0.001	< 0.001

<sup>1</sup>Indicates the intra-group comparison with that before treatment,  $P < 0.05$ .

<sup>2</sup>Indicates that compared with 1 month after treatment,  $P < 0.05$ .

<sup>3</sup>Indicates intra-group comparison with 3-mo treatment,  $P < 0.05$ .

VEGF: Vascular endothelial growth factor.

**Table 6 Interleukin-6 levels before and after treatment**

Group	Number of cases	IL-6 (ng/mL)			
		Prior treatment	One month of treatment	Three months of treatment	Treatment for 6 mo
Control group	65	76.31 ± 11.76	66.31 ± 11.76 <sup>1</sup>	52.34 ± 8.71 <sup>1,2</sup>	42.91 ± 5.93 <sup>1,2,3</sup>
Observation group	65	75.24 ± 12.03	60.12 ± 8.03 <sup>1</sup>	45.71 ± 7.62 <sup>1,2</sup>	34.73 ± 5.63 <sup>1,2,3</sup>
<i>t</i> value		0.196	4.476	3.981	8.309
<i>P</i> value		0.845	< 0.001	< 0.001	< 0.001

<sup>1</sup>Indicates the intra-group comparison with that before treatment,  $P < 0.05$ .

<sup>2</sup>Indicates that compared with 1 mo after treatment,  $P < 0.05$ .

<sup>3</sup>Indicates intra-group comparison with 3-mo treatment,  $P < 0.05$ .

IL-6: Interleukin-6.

**Table 7 Levels of soluble intercellular adhesion molecule-1 before and after treatment**

Group	Number of cases	sICAM-1 (ng/mL)			
		Prior treatment	One month of treatment	Three months of treatment	Treatment for 6 mo
Control group	65	373.37 ± 83.12	313.71 ± 54.62 <sup>1</sup>	236.42 ± 37.91 <sup>1,2</sup>	205.71 ± 20.31 <sup>1,2,3</sup>
Observation group	65	376.39 ± 83.83	280.18 ± 54.62 <sup>1</sup>	200.73 ± 37.91 <sup>1,2</sup>	180.31 ± 20.72 <sup>1,2,3</sup>
<i>t</i> value		-0.043	3.850	5.325	7.120
<i>P</i> value		0.966	< 0.001	< 0.001	< 0.001

<sup>1</sup>Indicates the intra-group comparison with that before treatment,  $P < 0.05$ .

<sup>2</sup>Indicates that compared with 1 mo after treatment,  $P < 0.05$ .

<sup>3</sup>Indicates intra-group comparison with 3-mo treatment,  $P < 0.05$ .

sICAM-1: Soluble intercellular adhesion molecule-1.

Studies have also shown[24] that intravitreal injection of conbercept combined with pan-retinal photocoagulation is more effective in treating severe non-proliferative DR with macular edema. Placental growth factor (PIGF) has various biological effects that induce endothelial cell proliferation and stimulate angiogenesis. It also increases vascular permeability by enhancing endothelial cell migration. Studies[25] have found that PIGF is highly expressed in pathological conditions, such as inflammation, tumors, tissue ischemia, and hypoxia, which may be related to the occurrence and development of DME. Another reason for the enhanced efficacy of the combined treatment of the two DME methods in this study may be associated with the inhibition of PIGF expression. VEGF is a glycoprotein with a molecular mass of 36 kDa to 46 kDa that induces cell mitosis and promotes angiogenesis. This is an important cellular factor associated with DME. When the retina is ischemic and hypoxic, related cells secrete a large amount of VEGF, which can interact with the tight junction proteins of endothelial cells, thereby destroying the structure and function of the blood-retinal barrier, eventually leading to retinal capillary leakage and macular edema. A critical component of the DME disease process is the inflammatory response, and various pro-inflammatory factors can affect each other and aggravate

Table 8 Levels before and after serum basic fibroblast growth factor treatment

Group	Number of cases	BFGF (g/L)			
		Prior treatment	One month of treatment	Three months of treatment	Treatment for 6 mo
Control group	65	52.16 ± 8.17	49.31 ± 7.28 <sup>1</sup>	40.21 ± 6.22 <sup>1,2</sup>	32.41 ± 3.21 <sup>1,2,3</sup>
Observation group	65	53.07 ± 8.02	44.12 ± 7.16 <sup>1</sup>	33.34 ± 5.98 <sup>1,2</sup>	23.62 ± 3.16 <sup>1,2,3</sup>
<i>t</i> value		-0.201	3.675	6.601	11.661
<i>P</i> value		0.841	< 0.001	< 0.001	< 0.001

<sup>1</sup>Indicates the intra-group comparison with that before treatment,  $P < 0.05$ .

<sup>2</sup>Indicates that compared with 1 mo after treatment,  $P < 0.05$ .

<sup>3</sup>Indicates intra-group comparison with 3-mo treatment,  $P < 0.05$ .

BFGF: Basic fibroblast growth factor.

DME[26].

Previous studies have demonstrated[27] that microglia are bifurcated and distributed in the inner retina under normal physiological conditions and mainly monitor retinal immunity. When there is local inflammation in the retina, microglia are activated, become amoebic, and gather at the site of inflammation, causing an inflammatory cascade, releasing many inflammatory mediators, and causing changes in vascular permeability. Additionally, inflammation can alter the function of retinal Müller cells, reduce the efficiency of intracellular fluid clearance, and cause fluid accumulation. IL-6 is a classic pro-inflammatory factor that induces apoptosis in retinal cells and increases their permeability by activating the nuclear factor- $\kappa$ B pathway. It is also an important inflammatory factor in DME[28]. sICAM-1 is an immunoglobulin, and in this study, the levels of VEGF, IL-6, sICAM-1, and BFGF in the vitreous fluid of the observation group were significantly reduced at three-time points after treatment-induced DME, and the efficacy was better. The intravitreal syringe of conbercept combined with laser photocoagulation improved the hypoxic state, reduced the inflammatory response, and enhanced treatment efficacy.

When conbercept and ranibizumab were compared in DME, it was found that both anti-VEGF drugs inhibited the expression of VEGF and IL-6[29]. The results showed that the use of conbercept in DR was safer and more credible. Therefore, to prevent DME, we should increase screening and health promotion for people at risk of DME (patients with poor glycemic control, combined hypertension, combined hyperlipidemia, kidney disease, anemia, and pregnancy) so that they know the specific means of preventing and cultivating good habits.

## CONCLUSION

Conbercept, combined with laser photocoagulation, is a highly effective therapeutic agent for DR. Its action mechanism may be achieved by downregulating the expression of VEGF, IL-6, sICAM-1, BFGF, and other genes. Although the study had positive results, it also had some limitations. Among them, the sample size is small, which makes the research results lack sufficient representativeness. Second, the short duration of the study may lead to the lack of long-term validation of the results. In order to better generalize the results of this study, follow-up studies need to focus on these limiting factors, which could help guide clinical treatment.

## ARTICLE HIGHLIGHTS

### Research background

China has a high prevalence of diabetes and a large base of diabetes. Diabetic retinopathy (DR) seriously affects the patients' quality of life.

### Research motivation

DR is an important condition affecting people's lives, health, and economic development. Therefore, effective and efficient treatment programs are required.

### Research objectives

To provide better treatment for DR with macular edema.

### Research methods

We selected 130 patients with diabetic macular edema who were hospitalized between January 2018 and May 2020 and assigned them to the following two groups according to treatment: the observation and control groups. The control group

was treated with laser photocoagulation, and the observation group received laser photocoagulation with an intravitreal injection of conbercept (65 patients in each group). Clinical efficacy was evaluated, and seven indicators were measured.

### Research results

The total efficacy rate in the observation group (93.85%) was higher than that in the control group (78.46%). In both groups, the BCVA correction effect was better after treatment, and that in the observation group was superior to that in the control group. Retinal thickness and CMT improved after treatment, and the observation group was superior to the control group. The levels of VEGF, IL-6, sICAM-1, and BFGF in both groups improved after treatment, and the observation group was superior to the control group.

### Research conclusions

In patients with macular edema, the combination of laser photocoagulation and intravitreal injections of Conbercept for DME is a more effective and safer way to improve vision, reduce retinal thickness, and lower intraocular cytokine VEGF levels.

### Research perspectives

It is more effective in treating DR with macular edema and is worthy of widespread promotion.

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## FOOTNOTES

**Author contributions:** Zhan HQ designed and performed the research and wrote the paper; Gu CY designed the research and supervised the report; Zhou JL designed the research and contributed to the analysis; Zhang J and Wu D provided clinical advice.

**Supported by** the Youth Project of Changzhou Health Commission, No. QN202129.

**Institutional review board statement:** This study was reviewed and approved by the Third People's Hospital of Changzhou.

**Informed consent statement:** This study has obtained informed consent from all patients.

**Conflict-of-interest statement:** The authors declare no conflict of interest.

**Data sharing statement:** Does not support sharing data with third parties.

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**S-Editor:** Chen YL

**L-Editor:** A

**P-Editor:** Chen YL

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