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Original Article

Preoperative intravitreal injection of conbercept improves the efficacy of neovascular glaucoma surgery

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Abstract: Objective: To investigate the therapeutic effects of intravitreal conbercept injection on neovascular glaucoma (NVG). Methods: Sixty-seven patients with NVG were retrospectively selected and divided into a study group (n=34), which received intravitreal conbercept injection combined with trabeculectomy and panretinal photocoagulation; compared to a control group (n=33), which received trabeculectomy and panretinal photocoagulation only. The therapeutic effects, visual acuity, intraocular pressure, grade of iris neovascularization (NVI), pain score, complication rate, and anterior chamber angle were compared between the two groups. Results: The total effective rate in the study group was significantly higher than in the control group (97.06% vs. 81.82%, P<0.05). After 1 month of treatment, the study group showed significantly better visual acuity improvement and intraocular pressure control compared to the control group (both P<0.05). At 6 months of treatment, the proportion of patients with NVI grade 0-1 in the study group was significantly higher (94.11% vs. 48.48%, P<0.05). The proportion of patients with an anterior chamber angle ≥ grade 2 was also higher in the study group (70.59% vs. 39.39%, P<0.05). Additionally, the incidence of complications in the study group was lower (14.71% vs. 39.39%, P<0.05). Conclusion: Preoperative intravitreal conbercept injection significantly improves NVI, visual acuity, and intraocular pressure control in patients with NVG, reduces the incidence of complications, and demonstrates both significant efficacy and good safety.

Keywords: Conbercept, intravitreal injection, neovascular glaucoma

Introduction

Neovascular glaucoma (NVG) is a secondary form of glaucoma typically caused by retinal ischemia and hypoxia. Its hallmark features include neovascularization of the iris (NVI) and angular neovascularization. Clinically, patients with NVG often present with severe eye pain, photophobia, corneal edema, irreversible vision loss, elevated intraocular pressure, corneal haze, moderate to severe conjunctival hyperemia, and angle adhesion. NVG is classified into three types based on its pathological changes: preglaucoma, open-angle glaucoma, and angle-closure glaucoma [1-3]. As the disease progresses, the anterior chamber angle typically shifts from open to closed, intraocular pressure continues to rise, and vision deteriorates, ultimately leading to blindness. Therefore, early intervention is critical for improving patient outcomes [4, 5].

The pathogenesis of NVG involves a complex interplay of factors, with over 40 known risk factors contributing to its development. A significant cause is the excessive secretion of vascular endothelial growth factor (VEGF) by retinal epithelial cells under ischemic and hypoxic conditions. This leads to vascular proliferation, increased permeability, and vascular remodeling. Elevated VEGF levels in the vitreous body promote the formation of new blood vessels on the iris surface and angle, which can form a fibrous vascular membrane. This neovascularization can contract and pull the iris epithelium around the pupillary edge, causing ectropion uvea and iris adhesion. Furthermore, it may impede aqueous humor outflow, leading to angle closure, increased intraocular pressure, and ultimately the development of NVG [6-8].

Current treatment strategies for NVG focus on controlling intraocular pressure and preserving

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visual function to prevent disease progression. These include standard filtering surgery and panretinal photocoagulation. The former aims to alleviate clinical symptoms, while the latter targets the elimination of neovascularization [9, 10]. However, many NVG patients present at advanced stages, making panretinal photocoagulation difficult. Prolonged intraocular pressure also causes irreversible damage, highlighting the need for more effective treatments to address NVI and enhance the efficacy of combined therapies [11].

Conbercept is a novel anti-VEGF fusion protein developed in China. It combines the extracellular domains of human VEGFR-1 and VEGFR-2 with the Fc segment of human immunoglobulin. Unlike traditional anti-VEGF drugs, conbercept has distinct structural advantages. Pharmacokinetic studies show that conbercept has a half-life of approximately 4.2 days in the vitreous body, with a moderate clearance rate compared to ranibizumab and bevacizumab, allowing for stable drug concentrations. Given the central role of VEGF in NVG pathogenesis and conbercept's potent anti-angiogenic properties, it holds considerable promise for NVG treatment. Recent clinical studies suggest that intravitreal conbercept injection can rapidly inhibit NVI, improving conditions for subsequent surgery [12]. However, systematic research on conbercept in combination with traditional surgery for NVG is limited, and further studies are needed to determine the optimal timing, dosage, and long-term safety of this treatment. This study demonstrates that preoperative intravitreal conbercept injection significantly reduces NVI, greatly improving both visual acuity and intraocular pressure in NVG patients.

Materials and methods

Case selection

A total of 67 patients (67 eyes) with NVG, treated at Ninghai First Hospital, were retrospectively selected as the study subjects. The patients were divided into a study group (n=34 cases, 34 eyes) and a control group (n=33 cases, 33 eyes) based on their treatment options.

Inclusion criteria: (1) Patients diagnosed with NVG clinically; (2) Patients with clear awareness and the ability to cooperate with study procedures; (3) Patients aged ≥18 years; (4) Complete medical records; (5) Patients presenting with NVI; (6) Monocular involvement.

Exclusion criteria: (1) Patients with psychiatric disorders; (2) Patients who had received other VEGF inhibitors prior to the treatment; (3) Patients with pre-existing vision loss or eye atrophy; (4) Patients with retinal detachment before surgery; (5) Patients with systemic diseases that could affect treatment outcomes; (6) Patients allergic to any drugs used in this study; (7) Patients with poor compliance to treatment; (8) Patients with secondary NVG due to ocular tumors; (9) Patients with severe cardiovascular or cerebrovascular diseases.

Elimination criteria: (1) Patients unable to continue the study due to illness or other factors; (2) Patients who withdrew from the study; (3) Patients lost to follow-up within 6 months post-surgery.

This study was approved by the Ethics Committee of Ninghai First Hospital, and all methodologies and experiments adhered to the Declaration of Helsinki.

Intervention methods

In the control group, patients underwent trabeculectomy combined with panretinal photocoagulation. The trabeculectomy procedure involved local anesthesia with eye drops followed by an injection of anesthetic around the eye. The skin and eyelid were disinfected, and a limbal-based conjunctival flap and limbal-based scleral flap were prepared. Cotton pads soaked with mitomycin C were placed under the scleral flap for 3 minutes, followed by rinsing with normal saline to dilute the mitomycin. Trabecular tissue and the surrounding iris were removed, and both the scleral and conjunctival flaps were sutured. Postoperative care included levofloxacin eye drops. Panretinal photocoagulation was performed 2 weeks after trabeculectomy, with a spot size of 200-300 μm, an exposure time of about 200 ms, and power of 200-300 mW. Areas subject to bleeding around the macular region were avoided. Each session involved 1,000 laser spots with a total of two cycles.

In the study group, patients received intravitreal injection of conbercept (Chengdu Kanghong

Biotechnology Co., Ltd., specification: 10 mg/mL, Approval No. S20130012) 3-7 days before trabeculectomy on the basis of treatments for the control group. The injection was performed by an experienced ophthalmologist. Levofloxacin eye drops (Santen Pharmaceutical (China) Co., Ltd., specification: 5 mL: 24.4 mg, Approval No. J20100046) were administered one day before the injection. After surface anesthesia, the eyelid was opened, and 0.05 mL of conbercept was injected into the vitreous body. The needle was withdrawn slowly, and the wound was compressed with a sterile cotton swab. Ofloxacin eye drops were applied on the second day post-injection. Three to seven days after the injection, slit-lamp examination (66 Vision Tech Co., Ltd., YZ5T) was used to observe a significant regression of NVI. Trabeculectomy and panretinal photocoagulation were then performed.

Data collection

Primary observation indicators: (1) Comprehensive clinical therapeutic effect: Based on related indicators such as intraocular pressure (IOP), the overall intervention effects were categorized into three groups: cure, effective, and ineffective.

Cure: No anti-glaucoma medications are required, and the patient's IOP is below 21 mmHg.

Effective: The IOP is maintained between 21-26 mmHg without medication, or below 21 mmHg with one anti-glaucoma drug.

Ineffective: The IOP remains above 30 mmHg after treatment, or exceeds 21 mmHg despite using two types of intraocular pressure-lowering medications.

The total effective rate was calculated as: Total effective rate = (number of cures + number of effective cases)/total number of cases × 100%.

(2) NVI before treatment and after 6-month treatment: NVI was evaluated before and after 6 months of treatment using a slit lamp.

Grade 1: Small amount of new blood vessels at the pupil edge in 1-2 quadrants.

Grade 2: New blood vessels in more than 3-4 quadrants.

Grade 3: New blood vessels in 1-3 quadrants and ectropion uveae.

Grade 4: Neovascularization in all four quadrants with ectropion uveae [13].

Secondary observation indicators: (1) Changes in vision acuity: Best-corrected visual acuity was assessed at baseline, and again at 1 week, 1 month, 3 months, and 6 months after treatment for both groups.

(2) Changes in IOP: IOP was measured at the same time points as visual acuity. Each measurement was repeated three times using a Goldmann tonometer, and the average value was taken as the final result. If the patient experienced corneal edema after treatment, an Icare-Pro Rebound Tonometer was used.

(3) Postoperative pain assessment: Pain levels were evaluated at baseline, and at 1 week, 1 month, and 3 months post-treatment using the Visual Analog Scale (VAS). The VAS is a 0-10 linear scale, with higher scores indicating more severe pain.

(4) Postoperative complications: Complications such as active hemorrhage, anterior chamber hemorrhage, vitreous hemorrhage, and choroidal detachment within 6 months post-treatment were recorded.

(5) Assessment of anterior chamber angle width: The anterior chamber angle width was assessed at baseline and 6 months post-treatment using a gonioscope (three-mirror lens). The Shaffer grading method was employed to evaluate angle opening, categorized into five grades:

Grade 0: Completely closed angle.

Grade 1: Extremely narrow angle (only the anterior trabecular meshwork is visible).

Grade 2: Narrow angle (trabecular meshwork visible).

Grade 3: Moderately open angle (ciliary body band visible).

Table 1. Comparison of baseline data between the two groups ($\bar{x} \pm s$)/[n (%)]

Data		Study group (n=34)	Control group (n=33)	t/χ^2	*P*
Gender	Male	17 (50.00)	17 (51.52)	0.015	0.901
	Female	17 (50.00)	16 (48.48)		
Average age (years)		41.01 ± 2.22	41.12 ± 2.03	0.211	0.834
Average course (years)		1.29 ± 0.21	1.31 ± 0.19	0.408	0.685
Education level	illiteracy	9 (26.47)	9 (27.27)	0.023	0.891
	Primary school	11 (32.35)	12 (36.36)		
	Junior high school	10 (29.41)	9 (27.27)		
	High school and above	4 (11.76)	3 (9.09)		
Marital status	Married	30 (88.24)	30 (90.91)	0.128	0.721
	Single	4 (11.76)	3 (9.09)		
Monthly income (yuan)	<1000	10 (29.41)	9 (27.27)	0.098	0.734
	1000-3000	11 (32.35)	12 (36.36)		
	>3000	13 (38.24)	12 (36.36)		

Table 2. Comparison of comprehensive therapeutic effect between the two groups [n (%)]

Group	Number of cases	Cure	Effective	Ineffective	Total effective rate
Study group	34	23 (67.65)	10 (29.41)	1 (2.94)	33 (97.06)
Control group	33	17 (51.52)	10 (30.30)	6 (18.18)	27 (81.82)
χ^2	-	-	-	-	4.157
P	-	-	-	-	0.041

Grade 4: Wide open angle (scleral spur visible).

The extent of peripheral anterior synechiae (PAS) was also recorded in clock hours.

Statistical methods

Data were analyzed using SPSS 22.0 software. Continuous data were expressed as mean ± standard deviation ($\bar{x} \pm sd$) and analyzed using independent sample t-test, paired t-test, or repeated measures analysis of variance (ANOVA), followed by LSD test. Categorical data were presented as number of cases and percentage [n (%)] and analyzed using the χ^2 test or Fisher's exact test. A *P* value <0.05 (two-sided) was considered statistically significant [14].

Results

Comparison of baseline data

The two groups were compared for general clinical data, including sex, average age, disease duration, education level, marital status, and monthly income. The differences between the two groups were not statistically significant (all P>0.05), indicating that the groups were comparable (**Table 1**).

Comparison of comprehensive therapeutic effects

In the study group, 23 eyes were cured, 10 eyes were effective, and 1 eye was ineffective, resulting in a total effective rate of 97.06%. In the control group, 17 eyes were cured, 10 eyes were effective, and 6 eyes were ineffective, with a total effective rate of 81.82%. The study group had a significantly higher total effective rate than the control group (P<0.05) (**Table 2**).

Comparison of vision acuity at multiple timepoints after treatment

There was no significant difference in visual acuity between the two groups before treatment (P>0.05). After treatment, both groups showed significant improvement in visual acuity. The visual acuity of the study group was significantly better than that of the control group at 1 month, 3 months, and 6 months of treatment (all *P*<0.05) (**Table 3**).

Table 3. Comparison of vision of the two groups ($\bar{x} \pm s$)

Group	Number of cases	Before treatment	At 1 week of treatment	At 1 month of treatment	At 3 months of treatment	At 6 months of treatment
Study group	34	2.18 ± 0.32	2.01 ± 0.23*	1.35 ± 0.29*	1.27 ± 0.32*	0.83 ± 0.21*
Control group	33	2.19 ± 0.33	1.99 ± 0.23*	1.54 ± 0.33*	1.44 ± 0.34*	0.95 ± 0.22*
t	-	0.126	0.356	2.505	2.108	2.284
P	-	0.9	0.723	0.015	0.039	0.026

Note: Compared with before treatment, *$P<0.05$.

Table 4. Comparison of intraocular pressure of the two groups ($\bar{x} \pm s$) (mmHg)

Group	Number of cases	Before treatment	At 1 week of treatment	At 1 month of treatment	At 3 months of treatment	At 6 months of treatment
Study group	34	40.21 ± 3.32	20.19 ± 3.21*	19.28 ± 3.14*	18.21 ± 3.12*	18.12 ± 2.19*
Control group	33	40.23 ± 3.29	26.01 ± 3.43*	23.81 ± 3.29*	21.87 ± 3.09*	21.71 ± 2.39*
t	-	0.025	7.173	5.767	4.823	6.414
P	-	0.98	<0.001	<0.001	<0.001	<0.001

Note: Compared with before treatment, *$P<0.05$.

Table 5. Comparison of iris surface neovascularization between the two groups before and after 6 months of treatment [n (%)]

Group		Grade				
		0	1	2	3	4
Before treatment	Study group (n=34)	0 (0.00)	0 (0.00)	10 (29.41)	20 (58.82)	4 (11.76)
	Control group (n=33)	0 (0.00)	1 (3.03)	9 (27.27)	20 (60.61)	3 (9.09)
χ^2	-			0.691		
P	-			0.441		
At 6 months of treatment	Study group (n=34)	11 (32.35)*	21 (61.76)*	2 (5.88)	0 (0.00)	0 (0.00)
	Control group (n=33)	4 (12.12)	12 (36.36)	17 (51.52)	0 (0.00)	0 (0.00)
χ^2	-			17.614		
P	-			<0.001		

Note: Compared with the control group at 6 months of treatment, *$P<0.05$.

Comparison of IOP at multiple time-points after treatment

No significant difference was found in IOP before treatment (P>0.05). After treatment, IOP decreased significantly in both groups, with values significantly lower than before treatment (P<0.05). The IOP in the study group was consistently lower than in the control group at 1 week, 1 month, 3 months, and 6 months post-treatment (all P<0.05) (**Table 4**).

Comparison of NVI before and 6 months after treatment

Slit-lamp examination revealed that before treatment, the study group had 10 cases with grade 2 neovascularization, 20 cases with grade 3, and 4 cases with grade 4; while the control group had 1 case with grade 1, 9 cases with grade 2, 20 cases with grade 3, and 3 cases with grade 4. There was no significant difference in NVI distribution between the two groups before treatment (P>0.05). After 6 months, the study group showed more significant regression of NVI, with 94.11% (32/34) of cases reaching grade 0-1, significantly higher than 48.48% (16/33) in the control group (P<0.05). The improvement in NVI grade was more pronounced in the study group (P<0.05) (**Table 5**).

Comparison of pain intensity

There was no significant difference in VAS scores between the two groups before treat-

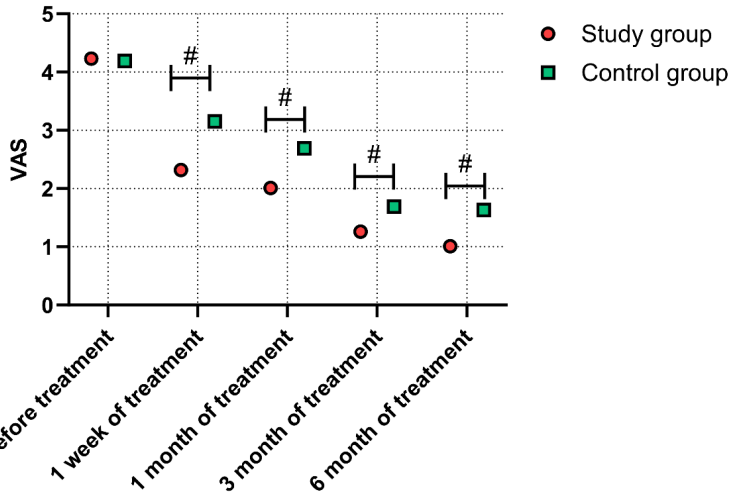

Figure 1. Comparison of pain scores between the two groups. Note: VAS: visual analog scale. #P<0.05.

ment (P>0.05). However, at 1 week, 1 month, and 3 months after treatment, the VAS scores in the study group were significantly lower than those in the control group (P<0.05) (**Figure 1**).

Comparison of complications

Follow-up and clinical records showed that within 6 months of treatment, the study group had 1 case of active bleeding, 1 case of hyphema, 2 cases of vitreous hemorrhage, and 1 case of choroidal detachment, totaling 5 cases, with an incidence of 14.71%. In the control group, there were 5 cases of active bleeding, 4 cases of hyphema, 3 cases of vitreous hemorrhage, and 1 case of choroidal detachment, totaling 13 cases, with an incidence of 39.39%. The incidence of complications was significantly lower in the study group compared to the control group (P<0.05) (**Table 6**).

Comparison of anterior chamber angle opening before and after treatment

No significant difference was observed in the distribution of angle opening between the two groups before treatment (P>0.05). After 6 months, 70.59% (24/34) of the study group had an anterior chamber angle of grade 2 or higher, significantly higher than 39.39% (13/33) in the control group (P<0.05). Both groups showed significant improvement in anterior chamber angle opening after treatment compared to baseline (P<0.05) (**Table 7**).

Discussion

NVG is a challenging condition in secondary glaucoma treatment [15, 16]. In early or open-angle glaucoma patients, only mild neovascularization appears in the iris, which can be managed effectively with anti-VEGF therapy or panretinal photocoagulation, delaying the progression of NVG [17, 18]. However, when neovascularization progresses to involve the entire iris, treatment becomes more difficult [19].

Filtration surgery or glaucoma valve implantation is often used to reduce intraocular pressure. However, clinical experience in recent years has shown that neovascularization increases the risk of complications such as anterior chamber hemorrhage and choroidal detachment after glaucoma filtration surgery. Glaucoma valve implantation, a more invasive procedure, is typically reserved for patients with absolute glaucoma. Although panretinal photocoagulation can inhibit neovascularization, it does not address the underlying excessive VEGF secretion in the vitreous of NVG patients [20-22]. Therefore, there is an urgent need to explore comprehensive treatment strategies. Some researchers have suggested that excessive VEGF expression in the vitreous can lead to pathological neovascularization on the retina and iris, thereby blocking the anterior chamber angle and inducing NVG [23]. Further studies have shown that VEGF can induce inflammation, promote the proliferation and migration of vascular endothelial cells, increase vascular permeability, and drive the formation of new blood vessels. Consequently, modulating VEGF overexpression offers a promising approach to accelerate neovascular regression in NVG patients [24].

This study demonstrated that intravitreal injection of conbercept significantly improved visual acuity and intraocular pressure following trabeculectomy combined with panretinal photocoagulation. The results suggest that conbercept plays a significant role in improving the visual

Table 6. Comparison of complications in the two groups after 6 months of treatment [n (%)]

Group	Number of cases	Active bleeding	Anterior chamber hemorrhage	Vitreous hemorrhage	Choroidal detachment	Total incidence
Study group	34	1 (2.94)	1 (2.94)	2 (5.88)	1 (2.94)	5 (14.71)
Control group	33	5 (15.15)	4 (12.12)	3 (9.09)	1 (3.03)	13 (39.39)
t	-	3.062	2.044	0.25	0.0	5.195
P	-	0.08	0.153	0.617	0.983	0.023

Table 7. Comparison of anterior chamber angle opening between the two groups before and after 6 months of treatment [n (%)]

Group		Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Before treatment	Study group (n=34)	18 (52.94)	12 (35.29)	4 (11.76)	0 (0.00)	0 (0.00)
	Control group (n=33)	17 (51.52)	11 (33.33)	5 (15.15)	0 (0.00)	0 (0.00)
χ^2	-			1.021		
P	-			0.336		
After treatment	Study group (n=34)	2 (5.88)*	8 (23.53)*	15 (44.12)*	7 (20.59)*	2 (5.88)*
	Control group (n=33)	8 (24.24)	12 (36.36)	10 (30.30)	3 (9.09)	0 (0.00)
χ^2	-			6.590		
P	-			<0.001		

Note: Compared with the control group after treatment, *$P<0.05$.

acuity and intraocular pressure in NVG patients. Previous studies have confirmed the excellent clinical efficacy of conbercept, a next-generation anti-VEGF drug, in treating fundus angiogenesis diseases. Its success in treating wet age-related macular degeneration offers strong theoretical support for its application in NVG management [25]. Moreover, clinical observations of patients in different stages of NVG have shown that conbercept provides significant therapeutic benefits in the early and middle stages of the disease, effectively reversing the pathological angiogenesis process [26]. This is consistent with the rapid regression of iris neovascularization observed in this study. The results indicate that conbercept is a highly targeted and safe VEGF inhibitor. Upon administration, it reduces vascular permeability, prevents new blood vessel formation, and promotes regression of existing neovascularization. Additionally, it inhibits postoperative scar tissue formation, improving surgical success rates and long-term visual outcomes and intraocular pressure control in NVG patients. In the study group, 32.35% and 61.76% of patients achieved grade 0 and grade 1 NVI, respectively, confirming these findings. It is worth noting that while conbercept injection effectively inhibits NVI, its effect should be prolonged through panretinal photocoagulation.

This study also explored conbercept's role in reducing postoperative complications. The results showed that the incidence of complications in the study group within 6 months after surgery was lower than in the control group, which can be attributed to the use of conbercept. As mentioned, although trabeculectomy significantly reduces intraocular pressure in NVG patients, complications like anterior chamber hemorrhage and choroidal detachment due to neovascularization can decrease the success rate of the procedure. The early application of conbercept effectively reduces neovascularization, improving conditions for subsequent surgery and significantly lowering postoperative complication rates.

Improvement in anterior chamber angle opening is a key indicator of treatment efficacy for neovascular glaucoma. In this study, a significantly higher proportion of patients in the study group had an anterior chamber angle grade of 2 or above after 6 months of treatment, compared to the control group. This suggests that intravitreal injection of conbercept can effectively promote the reopening of the anterior chamber angle. Mechanistically, conbercept exerts its therapeutic effect by inhibiting VEGF, facilitating the regression of NVI and reducing the formation of fibrovascular mem-

branes. This decreases traction on the peripheral iris and promotes the reopening of previously closed angles.

In conclusion, intravitreal injection of conbercept prior to surgery significantly reduces NVI, improving both visual acuity and intraocular pressure in NVG patients with high safety. There are some limitations in this study. First, it had a small sample size, which limits the comprehensiveness of the results. Second, there was a lack of long-term follow-up data, hindering the assessment of conbercept's long-term therapeutic effects in NVG patients. Future studies with larger sample sizes and extended follow-up periods are needed to provide a more robust theoretical foundation for the clinical treatment of NVG.

Disclosure of conflict of interest

None.

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