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Efficacy of Intravitreal Conbercept Injections in Macular Edema Secondary to Branch Retinal vein Occlusion

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Abstract:

Purpose: To assess the efficacy and safety of intravitreal conbercept injections in patients with macular edema (ME) secondary to branch retinal vein occlusion (BRVO).

Methods: The study included 33 patients (38 eyes) with ME secondary to BRVO who received intravitreal conbercept 0.05mL injections. The ophthalmological examination should be performed at least once a month during 6-month follow up, and central foveal thickness was measured with optical coherence tomography (OCT) to determine whether reinjection was needed. We compared the best corrected visual acuity (BCVA) between pretreatment and 1, 3 months after treatment, aslo the OCT results between pretreatment and 1 month after treatment. Moreover, we observed the occurrence of complications within 1 month after treatment.

Results: The logarithm of minimum visual acuity (VA) was 0.59 ± 0.21 at baseline, and improved to 0.35 ±0.12 after the first injection (P<0.01). The BCVA was statistically different

between baseline and 1, 3 months after treatment (P＜0.05), and the BCVA at 3 months after treatment was significantly higher than baseline (P<0.05). The central foveal thickness was also statistically different between baseline and 1 month after treatment (P<0.05). Only 5 patients (15.15%) had transient elevation of intraocular pressure, and no other obvious ocular adverse events were observed within 1 month after treatment.

Conclusion： Intravitreal injections of conbercept demonstrated a generally favorable short-term efficacy as well as safety in the treatment of ME due to BRVO based on OCT.

Keywords: Conbercept; Branch retinal vein occlusion ; Macular edema ; Optical coherence tomography.

1. Introduction

BRVO is common in people aged 65 or older, non-hereditary and occurs mostly in the temporal side, especially in the supraorbital quadrant, of which the most common is central vein obstruction accounting for about 36.9 %-69.4%.[1] ME is the main complication and the most common cause of visual impairment in BRVO.[2] Macular grid-like laser photocoagulation can reduce vascular leakage and ME, but the improvement of VA is limited, and ME persists in some patients after repeated treatment.[3] Anti-vascular endothelial growth factor (anti-VEGF) treatment ME secondary to BRVO showed marked efficacy in numerous studies.[4] Conbercept is an anti-VEGF drug independently developed by China with multiple targets, strong affinity and long duration of action characteristics, can block all subtypes of VEGF-A, VEGF-B and placenta growth factor, and completely penetrate the retina, which inhibits endothelial cell proliferation and neovascularization by competitively inhibiting the binding of VEGF to receptors and preventing the activation of VEGF family receptors.[5,6] Currently, the study of conbercept treat ME secondary to BRVO is rare. The present study shows that intravitreal conbercept injections in ME secondary to BRVO has achieved marked efficacy, the report is as follows.

2. Materials and Methods

2.1. Participants

The study included 33 patients (38 eyes) with ME secondary to BRVO who were treated in Qinghai University or Eye Hospital of China Academy of Chinese Medical Sciences between April 2014 and September 2014, of which including 15 males and 18 females. The patient's age ranged from 45 to 81 years with an average of 71.25 years . All patients were treated for the first time without OCT or other anti-VEGF therapy.

2.2. Treatments

All patients had optometry to check the BCVA at baseline, then intraocular injections of conbercept 0.05mL under sterile conditions in the operating room. The ophthalmological examination was carried out at least once a month during 6-month follow up, and central foveal thickness was measured with OCT to determine whether reinjection was needed. In the 38 eyes, 5 eyes (13.6%) did not require additional injection after the first injection, 17 eyes (44.74%) required 2 injections, 12 eyes (31.58%) required 3 injections and 4 eyes (10.53%) required 4 injections combined with laser treatment.

2.3. Outcome Measurements

Checked the patient's BCVA with standard VA chart at baseline and 1 or 3 months after treatment. Linear scan of the fundus was performed using Carl Zeiss OCT to measure macular retinal thickness, total volume of 6 mm macular area, pulse Choroidal neovascularization (CNV) and central foveal thickness at baseline and 1 month after treatment. The incidence of complications within 1 month after treatment was recorded, including anterior chamber inflammation response, corneal edema, and high intraocular pressure.

2.4. Statistical Analyses

The data of this study were analyzed using SPSS 16.0, and quantitative data expressed in $\bar{\chi} \pm s$. Single factor analysis of variance with repeated measurements was used before and after treatment, and the test level α=0. 05. A P value of <0. 05 was considered statistically significant.

3. Results

3.1. The change of BCVA before and after treatment

The logarithm of minimum VA was 0.59 ± 0.21 at baseline, significantly improved to 0.35 ± 0.12 1 month after treatment (P =0.001) , and 0.30 ± 0.14 3 months after treatment (P =0.001).

3.2. The change of OCT before and after treatment

The macular retinal thickness and total volume of 6 mm macular area had no statistically different between baseline and 1 month after treatment, however, the central foveal thickness had statistically significant different (P = 0.045), the average thickness was 211 ± 65 μm. Although the average foveal thickness (368 +126 um) increased 3 months after the first injection, it was still improved compared with the baseline. (Table 1).

Table1. Compared the OCT results before and after treatment (χ±s, n =25)

Times	Macular retinal thickness(μm)	Total volume of 6 mm macular area(mm^2)	central fovea thickness(μm)
baseline	320.08 ± 12.724	11.532 ± 0.447	572 ± 134
1 month after treatment	310.96 ± 9.304	11.108 ± 0.349	212 ± 97
P value	0.373	0.236	0.045

3.3. Incidence of complications within 1 month after treatment

The average number of injections were 2.5 ± 1.5 (including the first injection) during follow-up. Only 5 patients (15.15%) had transient elevation of intraocular pressure, and no obvious ocular adverse events such as endophthalmitis, uveitis, cataract progression, long-term high intraocular pressure etc. , were observed within 1 month after treatment.

4. Discussion

OCT is a non-invasive and two-dimensional imaging technology, which is safe and easy to operate. It has been widely used in the follow-up examination of various fundus diseases, and can objectively and quantitatively measure the retinal nerve fiber layer (RNFL) thickness and macular thickness with high accuracy and good repeatability.[7] In addition, it can also accurately observe the changes of macular morphology and central fovea thickness before and after treatment, especially pretreatment images with factors that significantly affect the automatic measurement, such as severe sub-retinal hyperplasia with or without sub-retinal neuroepithelial or pigmented epithelial fluid. Patients with ME secondary to BRVO are often associated with retina pigment epithelium detachment and fibrosis, so the pathological changes are more easily detected by OCT. Therefore, OCT should be routinely examined after each injection to clearly guide the repetitive treatment.[8]

Studies found that the VEGF levels in vitreous cavity of patients with retinal vein occlusion are significantly elevated, the overexpression of VEGF and its receptors is closely related to serum protein exudation, retinal thickening and ME.[9,10] Therefore, anti-VEGF expression can be used as an important therapy for ME secondary to BRVO. Previous studies showed that the use of anti-VEGF drugs has a certain effect on the VA and promote ME absorption for the BRVO patients.[11,12] Hikichi et al. suggested that the mechanism of intravitreal injection of anti-VEGF for the treatment of BRVO is that vascular occlusion induces upregulation of VEGF resulting in increased vascular permeability.[13] Conbercept is a fusion protein composed of the extracellular domain 2 of VEGF receptor 1 and extracellular domains 3 and 4 of VEGF receptor 2 combined with the Fc portion of the human immunoglobulin G1. Studies show that intravitreal conbercept injection can effectively improve the retinal function of patients with ME secondary to BRVO, which is conducive to rapid vision recovery and high safety. [14]

In this study, patients with ME secondary to BRVO received intravitreal conbercept injections, and measured central foveal thickness with OCT to determine whether reinjection was needed. The results showed that the logarithm of minimum VA was significantly improved one month after the first injection. The BCVA was statistically different between baseline and 1, 3 months after treatment, and the BCVA at 3 months after treatment was significantly higher than baseline. The central foveal thickness was also statistically different between baseline and 1 month after treatment. In addition, no obvious ocular adverse events were observed

within 1 month after treatment. The result showed that intravitreal injections of conbercept demonstrated a generally favorable short-term efficacy as well as safety in the treatment of ME due to BRVO based on OCT.

However, there were lso some shortcomings in this study: 1.The follow-up time was short, so it was not long enough to observe the degree of ME regression, VA and intraocular pressure changes; 2. There was no other drug control group, and it is impossible to rule out the improvement of vision due to self-healing factors; 3. The sample size is small, and there is a lack of large sample data analysis. Therefore, the long-term efficacy of intravitreal conbercept injection in the treatment of ME secondary to BRVO remains to be confirmed by larger, longer-observed studies.

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