The efficacy of intravitreal conbercept for chronic central serous chorioretinopathy: a retrospective clinical study

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Research Article

Keywords: Chronic central serous chorioretinopathy, Conbercept, Best-corrected visual acuity, Central macular thickness

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Abstract

Background: To evaluate the efficacy and safety of conbercept for patients with chronic central serous chorioretinopathy (CSC).

Methods: A retrospective clinical study. This study included twenty-seven patients (32 eyes) who were diagnosed with chronic CSC in our hospital from November 2015 to March 2018. All the patients received intravitreal conbercept with one intravitreal injection and pro re nata (PRN). Follow-up observations occurred at 1 week and 1, 2, 3, and 6 months after initial injection. Observed indicators included best-corrected visual acuity (BCVA), central macular thickness (CMT) and presence of subretinal fluid (SRF).

Results: During the 6-month follow-up, the mean number of injections required and performed was 1.50±0.67. The BCVA at the first visit, 1-week, 1-, 2-, 3- and 6-month follow-ups after the first injection was 0.44±0.26, 0.39±0.29, 0.38±0.29, 0.33±0.29, 0.31±0.30, and 0.31±0.29, respectively. The difference between the BCVA at each follow-up and the first visit was statistically significant ($F=9.717$, $P<0.05$). CMT at the first visit, 1-week, 1-, 2-, 3- and 6- month after first injection was 323.25±158.49μm, 263.78±122.52μm, 222.34±92.46μm, 195.63±69.18μm, 189.25±68.71μm, and 200.47±86.30μm, respectively. The difference between the CMT at each follow-up and the first visit was also statistically significant ($F=17.072$, $P<0.05$). Full resolution of fluid was achieved in 7 (21.9%) eyes at 1 month, 14 (43.8%) eyes at 2 months, 19 (59.4%) eyes at 3 months and 23 (71.9%) eyes at 6 months after the initial treatment of anti-VEGF injection. No severe adverse event was noted relevant to the therapy.

Conclusion: Intravitreal injection of conbercept can effectively reduce the CMT and improve the BCVA in chronic CSC in a short term of 6 months.

Keywords: Chronic central serous chorioretinopathy, Conbercept, Best-corrected visual acuity, Central macular thickness.

Background

Chronic central serous chorioretinopathy (CSC) commonly affects the posterior pole and is characterized by the serous detachment of the neurosensory retina and change in the retinal pigment epithelium (RPE), resulting from the leakage of RPE [1]. For most patients, the disorder of RPE is self-limited during weeks to months after the first onset. However, some patients may have difficulty in achieving full visual recovery if there is a persistent existence of subretinal fluid (SRF), serous retinal detachment or atrophy of the RPE [2]. Therefore, the therapeutic course should be taken to minimize the chances of this happening.

Currently, CSC is treated by photodynamic therapy (PDT), laser photocoagulation or intravitreal injection of anti-vascular endothelial growth factor (VEGF) [3-5]. Intravitreal injections of anti-VEGF, such as ranibizumab, bevacizumab, and aflibercept have been broadly used in chronic CSC [6-8]. Ranibizumab and bevacizumab are derived from a murine monoclonal antibody, while aflibercept is a recombinant fusion protein [9]. Francesco et al., Lim et al., Kim et al. and Inoue et al. all indicated that intravitreal

injection of bevacizumab resulted in improvement in best-corrected visual acuity (BCVA) and anatomic structures [2,6,10,11]. Bae et al. demonstrated that intravitreal ranibizumab may significantly enhance the mean logarithm of the minimum angle of resolution (logMAR) in BCVA and reduce the mean central macular thickness (CMT) by 6 months after the initial treatment [7]. These results showed that the intravitreal injection of anti-VEGF agents can be an effective treatment option for chronic CSC.

The clinical trials discussed above all relate to monoclonal antibodies. Few studies were found in the safety and effectiveness of intravitreal injections of recombinant fusion protein for chronic CSC. Similar to aflibercept, conbercept (Lumitin, Chengdu Kanghong Biotech Co., Ltd., Sichuan, China) is a recombinant fusion protein fused by VEGF receptors one and two and the Fc portion of the human immunoglobulin G1, which can block VEGF-B, placental growth factor and all VEGF-A isoforms [12]. Conbercept has been proven to be effective in age-related macular degeneration (AMD), central retinal vein occlusion and other macular disorders [9,13]. In the current study, we aim to investigate in the short-term efficacy and safety of conbercept in chronic CSC. Further studies on the long-term efficacy and safety are necessary.

Methods

This study reviewed 27 patients (32 eyes) diagnosed with chronic CSC who received intravitreal conbercept injection from November 2015 to March 2018 at the Hangzhou Branch of Eye Hospital of Wenzhou Medical University. Criteria for inclusion were: (1) age >18 years old; (2) presence of serous detachment of neurosensory retina and RPE on optical coherence tomography (OCT) (Spectralis, Heidelberg, Germany); (3) evidence of fluorescent leakage on fundus fluorescein angiography (FFA) (Spectralis, Heidelberg, Germany); (4) abnormal appearance of dilated choriocapillaris on indocyanine green angiography (ICGA) (Spectralis, Heidelberg, Germany); (5) symptom duration ≥6 months; and (6) follow-up period ≥6 months. Criteria for exclusion were: (1) secondary choroidal neovascularization; (2) accompanied with other eye diseases, such as AMD, polypoidal choroidal vasculopathy, glaucoma or ocular trauma; (3) previous treatments, including argon laser, photodynamic therapy, or vitreoretinal surgery.

All patients underwent complete ophthalmological work-up, including slit-lamp examinations, dilated fundus examinations, intraocular pressure measurements, BCVA testing, OCT, FFA, ICGA, and other testing as needed. The BCVA was evaluated by standard logarithmic visual acuity chart and is converted into LogMAR for statistical analysis. The CMT was assessed by a highly-qualified ophthalmologist using manual measurement of the distance between the inner limiting membrane and RPE at the fovea on OCT.

After initiation of conbercept (0.05ml/0.5mg) injection, patients underwent regular clinical examinations. Additional injections of conbercept were performed on a pro re nata (PRN) basis if (1) the BCVA loss was more than 0.2 logMAR; (2) or the SRF persisted or worsened compared to the last follow-up visit [7]. Safety was assessed by recording any ocular adverse events such as vitreous hemorrhage, retinal detachment or endophthalmitis during the study period. Follow-ups were at 1 week, 1, 2, 3 and 6 months

after the initial injection. Observed indicators included change in BCVA and CMT and presence of SRF. All participants signed informed consent before participating in the study. And the study was conducted in accordance with the tenets of the Declaration of Helsinki and approved by the ethics committee of hospital.

Statistical analyses were performed using SPSS version 19.0 (SPSS 19.0, Inc., Chicago, IL). All data were expressed as mean ± standard deviation. Serial changes in BCVA and CMT were compared using repeated measures analysis of variance. A P value of less than 0.05 was considered statistically significant.

Results

27 patients (32 eyes) with chronic CSC were enrolled. The mean age of these patients was 50.62±8.70 years old (range, 39–68 years; 20 men and 7 women). The mean logMAR BCVA was 0.44±0.26 at baseline, 0.39±0.29 at the 1-week follow-up, 0.38±0.29 at the 1-month follow-up, 0.33±0.29 at the 2-month follow-up, 0.31±0.30 at the 3-month follow-up, and 0.31±0.29 at the 6-month follow-up. The difference between the BCVA at each follow-up and the first visit was statistically significant ($F=9.717$, $P<0.05$) (Figure. 1). As a result, treatment of conbercept injection improved the logMAR BCVA at 2-month($P=0.005$), 3-month($P=0.001$) and 6-month follow-ups($P=0.00$

The mean CMT was 323.25±158.49μm at baseline, 263.78±122.52μm at the 1-week follow-up, 222.34±92.46μm at the 1-month follow-up, 195.63±69.18μm at the 2-month follow-up, 189.25±68.71μm at the 3-month follow-up, and 200.47±86.30μm at the 6-month follow-up., The difference between the CMT at each follow-up and the first visit was also statistically significant ($F=17.072$, $P<0.05$). With the initial treatment of conbercept, the mean CMT was substantially reduced at each follow-up continuously($P<0.05$) (Figure. 2).

Initially, presence of SRF was found in all 32 eyes. Full resolution of fluid was achieved in7 (21.9%) eyes at 1 month, 14 (43.8%) eyes at 2 months, 19 (59.4%) eyes at 3 months and 23 (71.9%) eyes at 6 months after the initial treatment of anti-VEGF injection.

During the 6-month follow-up, the average number of injections required was 1.50±0.67 (range, 1–3), and no severe adverse events were noted relevant to the therapy.

Discussion

A variety of factors were found to be associated with chronic CSC, including type A personality, stress event, elevated levels of corticosteroids and genetic susceptibility [14]. Nonetheless, the essential pathogenesis of chronic CSC remained undiscovered with controversy. It is generally accepted that the dysfunction of RPE and the choroidal vascular hyperpermeability primarily lead to the detachment of the RPE in chronic CSC patients [15]. Therefore, some proposed on the potential efficacy in anti-VEGF treatment in chronic CSC given its anti-permeability properties in decreasing the choroidal vascular

hyperpermeability [16]. Currently, several kinds of anti-VEGF agents have been in use. Yun et al. demonstrated that intravitreal injection of aflibercept can significantly decrease subfoveal choroidal thickness more than ranibizumab in the treatment of neovascular AMD due to their difference in biochemical structures [17]. Since the CSC is known to be a type of pachychoroid disease associated with choroid dysfunction [18], it is a possibility that the application of intravitreal conbercept may be effective in treatment for the chronic CSC.

In our study, 30 (94%) out of 32 eyes had stable or improved vision at the time of the last follow-up. A mean reduction in CMT was found to be 122.7μm at 6 months. Overall, “1+prn” treatment protocol has demonstrated the efficacy of intravitreal injection of conbercept in improving BCVA and reducing CMT in the chronic CSC patients over a period of 6 months. The study defined the complete resolution of SRF on the OCT as high responders (HRs). At the 6-month follow-up, there were 23 (71.9%) HRs without any adverse events. This result proved the efficacy and safety of intravitreal injection of conbercept in CSC patients in a short term. Further study is required in determining efficacy and safety in a more frequent treatment regimen, such as monthly injection or a 3+PRN treatment. The pathophysiology in the treatment of CSC with anti-VEGF therapy is not yet completely understood. Lim et al. discovered that the VEGF in the aqueous was significantly correlated with the symptom duration [19]. Thus, we can generally believe that anti-VEGF therapy plays a significant role in chronic CSC. Recent published studies in small case series showed that intravitreal injections of bevacizumab or ranibizumab resulted in visual improvement and CMT reduction without adverse events. Lim et al. also indicated that the bevacizumab injection may help to improve visual acuity and anatomical results [6]. Another study from Kim et al. reported 42 patients who were treated with intravitreal injections of bevacizumab had significant reduction in CMT, SRF height and SRF volume with no visual improvement at the last follow-up. 60% of them achieved complete resolution at a mean follow-up of 8.6 months [10]. Inoue et al. reported results of one-year follow-up examinations. Their study demonstrated that intravitreal injection of bevacizumab was effective in maintaining vision and improving serous retinal detachment [11].

In this study, there are still several limitations of relatively short-term follow-up period, small sample size and lack of a control group. Further investigations are expected in both a larger sample and a longer term of study period. The comparison between efficacy of conbercept injection and PDT may be compared to determine the most beneficial first-line treatment for chronic CSC.

Conclusions

In summary, the results of our study demonstrated significant improvement in visual acuity and anatomic structures with intravitreal injections of conbercept in chronic CSC. Intravitreal injections of conbercept should be considered in treating chronic CSC patients.

Abbreviations

CSC: central serous chorioretinopathy; PRN: pro re nata; BCVA: best-corrected visual acuity; CMT: central macular thickness; SRF: subretinal fluid; RPE: retinal pigment epithelium; PDT: photodynamic therapy; VEGF: vascular endothelial growth factor; logMAR: logarithm of the minimum angle of resolution; AMD: age-related macular degeneration; OCT: optical coherence tomography; FFA: fluorescein angiography; ICGA: indocyanine green angiography

Declarations

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Not applicable

Availability of data and materials

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

Authors' contributions

Design of the study (JM, and LS); data collection (CZ, and YS), analysis and interpretation of the data (CZ, JM, and JL), preparation, review and approval of the manuscript (JM, CL, YC, and JT). All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study followed the tenets of the Declaration of Helsinki and was approved by the ethical committee of Eye Hospital of Wenzhou Medical University. Informed consent was obtained from each patient before the study.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Figures

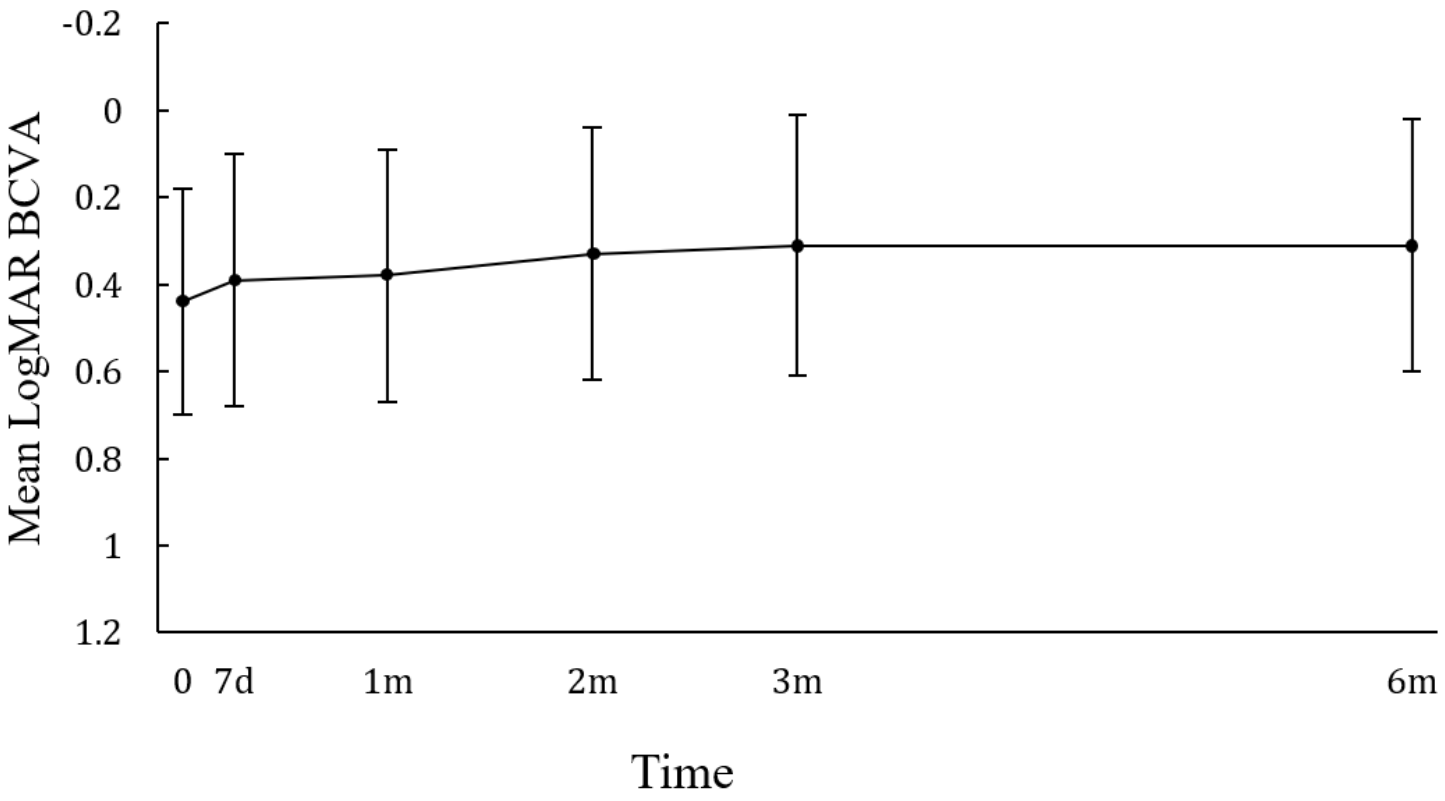

Figure 1

Change in BCVA from baseline to Month 6.

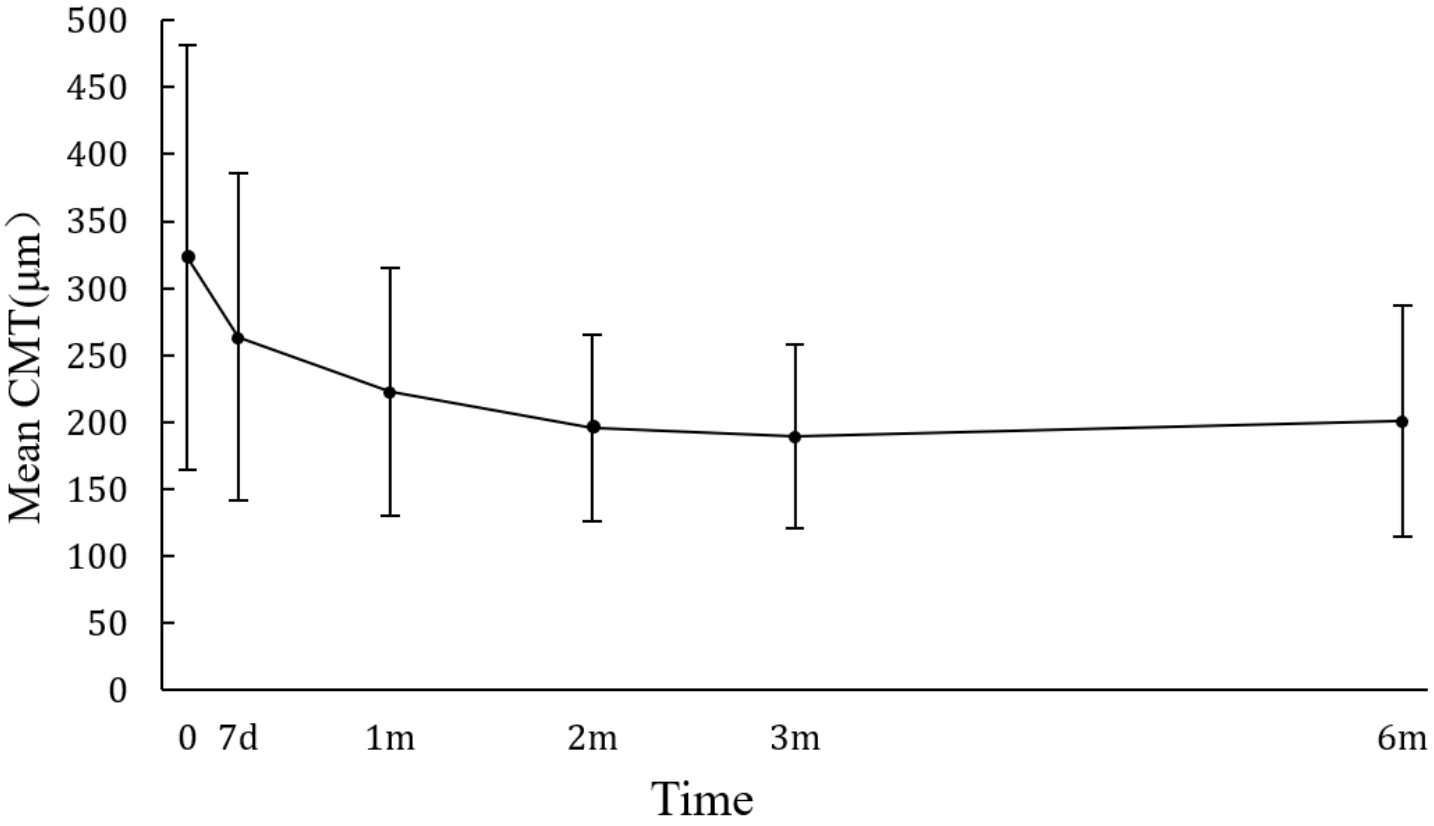

Figure 2

Change in CMT from baseline to Month 6.