

ORIGINAL RESEARCH

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Visual recovery comes after anatomical recovery after intravitreal aflibercept treatment in macular edema secondary to branch retinal vein occlusion

Alper Halil Bayat, Burak Erden, Akin Cakir, Seyma Gulcenur Ozturan, Selim Bolukbasi, Mustafa Nuri Elcioglu

Okmeydani Research and Training Hospital, University of Health Sciences, Department of Ophthalmology, Istanbul, Turkey

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Abstract

To determine the time of anatomical and visual responses of intravitreal aflibercept (IVA) injections in patients with naive macular edema (ME) due to branch retinal vein occlusion (BRVO). 54 eyes of 54 patients who had three IVA injections after BRVO were retrospectively studied. All of the patients had three monthly IVA injections. SD-OCT was performed at the initial visit and one month after every injection. Changes in central macular thickness (CMT), best corrected visual acuity (BCVA) were determined. Results: 28 of 54 patients were women and 26 of 54 patients were man. Mean age was 62.56 ± 2.35 years. Mean BCVA of the patients was $\log\text{MAR } 1.00 \pm 0.13$ and the mean CMT was $476 \pm 35 \mu\text{m}$. After first injections; mean BCVA and CMT were improved to $\log\text{MAR } 0.73 \pm 0.19$, $279 \pm 15 \mu\text{m}$ respectively. These improvements were statically significant ($p=0.047$ and $p=0.000$ respectively). After second injections there was not any improvement in BCVA or CMT. The mean BCVA $\log\text{MAR } 0.75 \pm 0.18$ and mean CMT $279 \pm 10 \mu\text{m}$ ($p=0.725$ and $p=0.991$). After third injections mean CMT was $267 \pm 6 \mu\text{m}$ and mean BCVA was $\log\text{MAR } 0.58 \pm 0.15$. Although after third injections, CMT did not change but BCVA was statically significant improved ($p=0.77$ and $p=0.036$ respectively). Visual recovery comes after anatomical recovery after intravitreal aflibercept injections in patients with naive ME due to BRVO.

Keywords: Branch retinal vein occlusion, macular edema, aflibercept treatment, anatomical recovery, visual recovery

Introduction

Retinal vein occlusion (RVO) is the second most common type of retinal vascular disease after diabetic retinopathy [1,2]. RVO can be classified as central retinal vein occlusion (CRVO) or branch retinal vein occlusion (BRVO). Macular edema (ME) is the main cause of visual impairment in patients which has RVO [1-4]. There are some treatments for macular edema such as intravitreal dexamethasone implants, laser treatment, and intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) agents. Positive clinical outcomes have been reported on successful use of anti-VEGF such as bevacizumab and ranibizumab [4-13]. After these drugs, aflibercept has been used for ME due to RVO [14-15]. There are some studies in literature about aflibercept usage in ME due to BRVO.

But all of them are switch studies. There are not enough real life studies about aflibercept treatment in ME due to BRVO with naive patients. We aimed to evaluate the effectiveness of aflibercept

in patients with naive ME due to BRVO. We want to determine the time of anatomical and visual responses of IVA injections in patients with naive ME due to BRVO.

Materials and Methods

This retrospective study was conducted in accordance with the Declaration of Helsinki. All necessary authorizations were obtained from the Institutional Review Board of Okmeydani Research & Training Hospital, Istanbul, Turkey.

54 eyes of the 54 patients with treatment-naive acute ME due to BRVO were studied. All of the patients who had intravitreal aflibercept (IVA) injections at Okmeydani retrospectively studied. Patients with $\text{CMT} > 300$ in OCT were treated. All of the patients received 3 consecutive monthly IVA injections. Patients with a history of cerebral infarction, anti-VEGF therapy, dexamethazone therapy, vitrectomy, uveitis, glaucoma or other vitreoretinal diseases were excluded.

All of the patients had standard ophthalmic examinations before treatment and post treatment (first, second and third month and at the final visit). The examinations included slit-lamb microscopy, BCVA, tonometry, SD-OCT, indirect ophthalmoscopy. The BCVA

was measured with Snellen chart, and the decimal visual acuity was converted to the logarithm of the minimal angle of resolution (logMAR) units for the statistical analyses. The OCT was performed on SD-OCT (Cirrus HD-OCT; Carl Zeiss Meditec).

Statistical analyses were performed using the SPSS software version 21. The variables were investigated using means and standard deviations for normally distributed variables. When investigating the changes in BCVA and CMT by time; repeated measures of analysis of variance test (ANOVA) was used. A $P < 0.05$ value was accepted statically significant.

Results

28 of 54 patients were women and 26 of 54 patients were man. Mean age was 62.56 ± 2.35 . Mean BCVA of the patients was $\log\text{MAR } 1.00 \pm 0.13$ and the mean CMT was $476 \pm 35 \mu\text{m}$. Table-1 shows the baseline characteristics of the patients.

Table 1. Baseline characteristics of the patients

Age	62.56 ± 2.35 years
Gender	28 women, 26 men
Lens status (phakic, psuedophakic)	15/39
Duration of symptoms (days)	17.2 ± 6.1
Central foveal thickness (μm)	476 ± 35
Best corrected visual acuity (logMAR)	1.00 ± 0.13

After first injections; mean BCVA was improved to $\log\text{MAR } 0.73 \pm 0.19$ ($p = 0.047$). After second injections there were not any improvement in BCVA. The mean BCVA was $\log\text{MAR } 0.75 \pm 0.18$ ($p = 0.725$). After third injections mean BCVA was improved to $\log\text{MAR } 0.58 \pm 0.15$ ($p = 0.036$). From initial to third injections the improvement in BCVA was statically significant ($p = 0.003$). The change in BCVA over time was depicted in Figure 1.

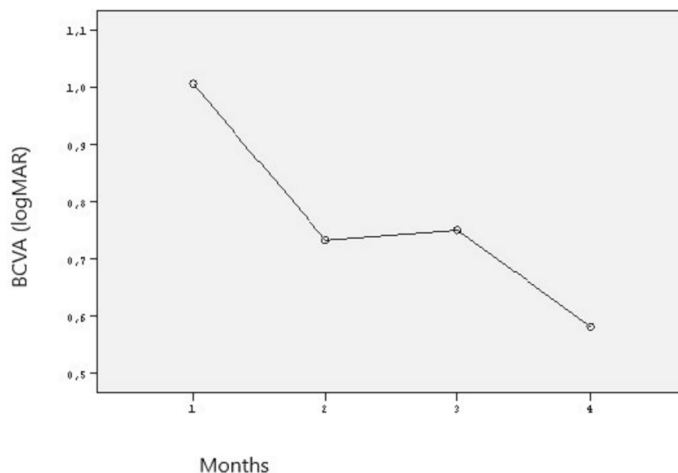


Figure 1 The changes in BCVA over time

After first injections; CMT was improved $279 \pm 15 \mu\text{m}$ ($p = 0.000$). After second injections there were not any improvement CMT. The mean CMT was $279 \pm 10 \mu\text{m}$ ($p = 0.991$). After third injections mean CMT was $267 \pm 6 \mu\text{m}$. There was not any improvement from the second injections to third injections ($p = 0.77$). From initial to the final visit the improvement in CMT was statically significant

($p = 0.000$). The change in CMT over time was depicted in Figure 2.

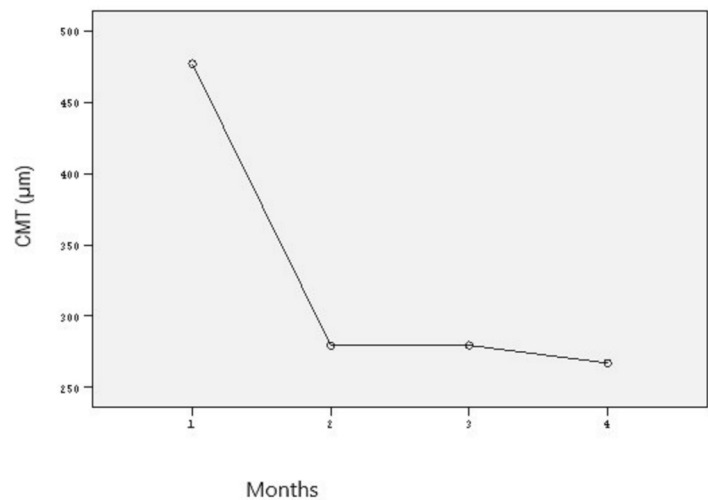


Figure 2. The changes in CMT over time

Discussion

For a long time, argon laser photocoagulation has been used in BRVO and has been recommended as a treatment method for reducing macular edema and increasing visual acuity [16-17]. Then anti-VEGF therapy has started to be used and according to important results of ranibizumab and aflibercept in the BRAVO and VIBRANT studies, anti- VEGF has become the most effective drugs for the treatment of BRVO associated ME [4,18-19]. Several studies suggest that VEGF is a major mediator for ME in BRVO. Ischemic retinas express VEGF and vitreous fluid levels of VEGF was correlated with the severity of macular edema in patients with BRVO [20-21]. Aflibercept is a fully human, recombinant receptor fusion protein with a VEGF binding affinity higher than ranibizumab or bevacizumab with a longer duration of effect in the eye and it displays a prolonged VEGF inhibition in comparison with the other VEGF-antagonists ranibizumab and bevacizumab in retinal pigment epithelium/choroid organ cultures. It is also important that it binds other angiogenic factors including placental growth factors [22-25]. The efficacy of aflibercept, an anti-VEGF binding protein, was demonstrated in the VIBRANT phase 3 trial. This study demonstrated, aflibercept (2 mg) treatment was found to be much more effective than laser treatment in macular edema secondary to BRVO. And VIBRANT study has shown important treatment modality which results in markedly functional and anatomical improvement [19,24]. In VIBRANT study patients had anatomical gain more than $200 \mu\text{m}$ after first injection. While this gain was $280 \mu\text{m}$ at 6th month. If you look carefully, you will see that the vast majority of the anatomical gains come from the first injections. The patients had approximately 12 letters gain after first injection, while it was 17 letters at 6th month. If you look carefully, you will see that visual gain comes after anatomical gain in VIBRANT study too.

GALILEO study was about efficacy of aflibercept in pateints with ME secondary to central retinal vein occlusion. In that study, six monthly aflibercept injections were performed. After first injection, patients had approximately $400 \mu\text{m}$ anatomical gain, while it was $448 \mu\text{m}$ at 6th month. When we consider visual gain, the patients had approximately 12 letters gain after first injection, while it was 18 letters at 6th month [26]. This studies confirmed that patients

have fast anatomical recovery after first aflibercept injection in ME due to RVO, while anatomical recovery takes some more time.

In Errol et al.'s study the mean age was 58.6 and 62.56 in our study [27]. Like our study the mean age was 63.3 in Wang JK et al. study, and according to them CMT significantly decreased after the first injection like our and VIBRANT trial [19,25]. We found that there was no significant difference of CMT was found in subsequent injections. After first injection, the CMT decreased significantly, while the visual acuity improved markedly. There was no significant change in CMT at subsequent injections, while visual acuity continued to increase. This result may make us think although anatomical recovery be maintained, visual recovery takes some times. This important outcome shows how important the continuity of treatment is. We should not terminate or switch the treatment, thinking that the vision has not increased enough. Before terminate or switch the treatment, we need to complete required injection dose.

Conclusion

In conclusion, patients have fast anatomical recovery after first aflibercept injection in ME secondary to BRVO, while visual recovery takes more time.

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None of the authors has conflicts of interest or financial interest.

Competing interests

The authors declare that they have no competing interest

Financial Disclosure

The financial support for this study was provided by the investigators themselves.

Ethical approval

All necessary authorizations were obtained from the Institutional Review Board of Okmeydanı Research & Training Hospital

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