Original Article

Anti – VEGF Treatment in Macular Edema Due to Retinal Vein Occlusion

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Abstract

CRVO and BRVO can cause macular edema with the decrease of visual acuity. Treatment with anti-VEGF for macular edema in patients with RVO is now the best choice to improve the visual acuity and the life quality of the patients. Considering the role of VEGF as one of the main factors in the development of macular edema, this study aims to examine the anatomical and functional long-term effects of the use of anti-VEGF intravitreal drugs in the treatment of secondary macular edema caused by RVO.

This is a retrospective study, where 25 patients diagnosed with macular edema following RVO were included. Patient Visual acuity with Snellen chart, intraocular pressure, fluorangiography, and OCT was done on all the patients in their first visit. The patients were treated with intravitreal Aflibercept and were followed up for 2 years.

The results of this study revealed that aflibercept was effective in patients that have macular edema following RVO, in maintaining or improving visual acuity in a long-term follow-up of 26.2 ± 7.6 months and in terms of reducing macular edema. Compared to one-third of CRVO patients, BRVO patients appear to have a better prognosis because 75% presented ≥6 / 12 visual acuity at the end of the follow-up period. Our results also suggest that intraretinal fluid and macular cystoid edema with increased TCF were associated with adverse visual outcomes. The integrity of outer retinal layers influences the improvement of BCVA, the damage in the photoreceptor can lead to poor visual acuity.

Keywords: Branch vein occlusion, Intravitreal injections, Macular edema, Albania

Introduction

Macular edema from CRVO and BRVO is caused by an increase in venous pressure in the perifoveal capillaries which leads to damage of the endothelium of the capillary [1]. From this, a local leakage and macular edema will be formed in the retina [2, 3]. Chronic macular edema from CRVO is associated with a poor visual prognosis [4]. In this study, we aim to evaluate the anatomical changes in patients who are treated with intravitreal injection (anti-VEGF) and in patients that are untraited with anti – VEGF.

Materials and Methods

Population

The study was conducted based on a retrospective observational study of a cohort of 25 treatment patients (25 eyes) naive with macular edema following RVO, treated with intravitreal Aflibercept. The patients were examined in the ophthalmology clinic at the ORL-Ophthalmology department, Faculty of Medicine, University of Medicine, Tirana, in a timeframe between June 2015 and June 2017 (23 months). All patients were diagnosed with macular edema due to RVO.

Inclusion Criteria

Inclusion criteria were age > 18 years, transparency of dioptric tools to obtain a good quality image in OCT, Snellen visual acuity between 20/40 and 20/300 in the examined eye. Anatomical criteria for inclusion required a CRT (central retinal thickness) of ≥ 320 µm in OCT. All patients included in this study were treated with at least 3 intravitreal anti-VEGF injections of 2 mg Aflibercept. When the ischemic forms were accompanied by retinal neovascularization, pan-retinal/scatter photocoagulation laser was used. All patients underwent a 2-year follow-up.

Exclusion Criteria

- Previous intravitreal injections
- Patients who had previously undergone systemic anti-VEGF therapy for neoplastic pathology.
- Presence of co-morbidity.

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- Eyes that had previously undergone vitrectomy, dense cataracts, uveitis, previous laser photocoagulation.

Clinical Examinations

The population underwent clinical and instrumental ophthalmological studies, designated to identify useful information for the study. Investigations aimed at assessing ocular involvement were as follows:

- Anamnestic and demographic: family and pathological anamnesis was investigated
- Spatial visual acuity (VA): assessed by Snellen optotypes and using the best possible correction (BCVA = Best Corrected Visual Acuity).
- Biomicroscopy with a slit lamp
- Fundus oculi: was evaluated through indirect ophthalmoscopy, using convex lenses with high magnification, suitable for obtaining a wide field of view. Before the examination, mydriatic drops (1% tropicamide) were instilled into the eye to enlarge the pupil, giving a better view of the fundus.

At each visit, visual acuity of the best visual acuity (BCVA) was measured using the Snellen chart. Intraocular pressure with applanation, an OCT, and a clinical eye exam, was done to all the patients every 3 months to identify intra/subretinal fluid, the presence of vitreous macular traction, and type of macular edema (cystoid or diffuse). At the first visit of each patient, we performed an FFA (Fluorescein angiography) to confirm the diagnosis and evaluate the ischemic index. Ischemic forms of CRVO were defined as such when the non-vascularized surface appeared larger than a 10-disc diameter (DD).

Table 1. Demographic data of patients with macular edema from CRVO

Woman	**11 (44%)**
Open-angle glaucoma	3 (36%)
Hypertension	17 (68%)
Diabetes mellitus	3 (12%)
Hyperlipidemia	15 (60%)
Smoking	16 (64%)
Ischemic type	7 (28%)
Duration of RVO < 3 months	17 (68%)

Results and Discussion

Table 2. Demographic data of patients at the first visit

	Patients with RVO (CRVO 12 eye & BRVO 13 eye)
Age	62.3 ± 7.1
BCVA (Snellen)	20/80
A central thickness of the fovea (µm)	586.9 ± 141.3
Gender	
Men	14 (56%)

Based on the subjects' data, the predominant pathology is of the non-ischemic type (78% of the cases), most commonly in males (12% more), as well as with main accompanying pathologies (by incidence) such as hypertension (68%), smoking (64%), hyperlipidemia (60%), open-angle glaucoma (36%) and diabetes mellitus (12%). The duration of RVO, in 68% of the cases, has been shorter than three months **(Table 2)**.

Table 3. Evolution of visual acuity over 2 years

	Month0	**Month 1**	**Month 2**	**Month 3**	**Month 6**	**Month 9**	**Month 12**	**Month 18**	**Month 24**
BCVA	20/80	20/63	20/63	20/63	20/63	20/63	20/63	20/63	20/63
n	25	25	25	25	25	25	25	25	25

The visual acuity was 20/80 in month 0. As evident in **Table 3,** the evolution of acuity has improved, reaching the maximum peak of 20/63 within the first month. Despite continued therapy, there were no further improvements in visual acuity by the end of the follow-up period.

Table 4. Evolution of central fovea thickness over 2 years

	Month 0	**Month 1**	**Month 2**	**Month 3**	**Month 6**	**Month 12**	**Month 18**	**Month 24**
TCF (µm)	587	472	408	373	310	327	301	345
n	25	25	25	25	25	25	25	25

The average TCF was 586.9 ± 141.3 µm in month 0. In **Table 4** we can see the TCF over time. TCF was significantly reduced by 282 µm compared to month 0, whereas the maximum reduction of TCF was observed in the 18th Month (-286 µm). The average follow-up period was 26.2 ± 7.4 months.

On average, the number of injections was 8.6 ± 3.1. In the first year, patients received an average of 5.1 Aflibercept injections. Whereas, the number of injections was 2.8 during the second year. Patients with CRVO received more injections than patients with BRVO. After 2 years, the number of patients having recurrent macular edema was

higher in patients with macular edema from CRVO than patients with macular edema from BRVO. After the statistical analysis, it was evident that old age, the presence of intraretinal fluid, cystoid edema, ischemic type of thrombosis were associated with unfavorable prognosis of visual acuity. 5 (41%) patients with CRVO and 2 (15%) with BRVO developed retinal neovascularization.

The main finding of this study was that aflibercept appears to be a safe and effective pharmacological agent for the treatment of macular edema caused by RVO. The effects of the treatment were evident in a period from 26.2 ± 7.4 months. With regards to visual acuity, it was noted that approx. 55% of the patients had a BCVA of ≥ 6/12. The macular edema resolution was observed in about 2/3 of the patients. Moreover, it is evident from the data that about 30% of patients needed intravitreal injections well beyond the second year of the follow-up period, due to recurrent macular edema.

In their study, BRAVO and CRUISE determined the 6 intravitreal injections effect with 0.5 mg ranibizumab, 0.3 mg ranibizumab in patients with macular edema from, BRVO and CRVO. After 12-month, their results showed a BCVA improvement [5].

COPERNICUS noted a gain of ≥ 15 BCVA logMAR letters of 56.1% versus 12.3% (P <0.001) in patients on the 24th week in the aflibercept injections groups respectively, compared to 55.3% and 49.1% versus 30.1% and 23.3% (P <0.001 for both) of patients in 52 and 100 weeks in the aflibercept injections groups, respectively 10 [6]. In this study, patients received intravitreal aflibercept based on their needs after 24 weeks.

GALILEO results showed the progress of ≥ 15 BCVA logMAR letters from 60.2% and 22.1% in the 24th week, in patients treated with aflibercept and sham injections (P <0.0001) respectively, and a TFC decrease of 448.6 mm compared to 169.3 mm (P <0.0001) in the aflibercept and sham injections groups, respectively [7]. Both studies demonstrated the efficacy of aflibercept in treating macular edema due to CRVO, but they also showed that it was necessary to continue for a long time anti-VEGF injection to control macular edema in many patients that have CRVO [8].

In our study, the disruption of the outer limiting membrane was related to a decreased visual acuity. Other studies reported that patients with intact IS / OS zone gained 18 logMAR letters. Patients with significant IS / OS anomalies gained only 4 logMAR letters (P,0.01) 1 month after the first injection of 0.5 mg ranibizumabm or 1.25 mg bevacizumab [9]. The integrity of the outer retinal layers influences the improvement of BCVA. Damage in the photoreceptor can lead to a poor visual acuity [1], even in our study we have found a poor visual prognosis in patients with damage of photoreceptor layer in OCT.

Our results suggest that intraretinal fluid and macular cystoid edema with increased TCF were associated with adverse visual outcomes. If the edema persists after the injection, this can indicate that the disease is still active and more injection is needed for the disorder. The poor visual outcome can affect the quality of life [10].

Conclusion

We can say that aflibercept injection was effective in patients presented with macular edema from RVO. The visual acuity was improved at 26.2 ± 7.6 months, where 75% of the patients had a better prognosis. Patients with disrupted photoreceptor zone had poor visual outcomes.

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