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Original Research Article

Changes in Foveal Avascular Zone Area in Patients with Retinal Vein Occlusion after Intravitreal Ranimuzumab

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Abstract:

Background: Macular edema due to retinal vein occlusion (RVO) is a significant cause of visual loss. The conventional treatment for this condition is intravitreal injections (IVI) of anti-vascular endothelial growth factor (VEGF). The study aimed to look into changes in foveal avascular area (FAZ) and visual gain in patients with macular edema caused by retinal vein occlusion (RVO) who was treated with intravitreal ranibizumab, an anti-VEGF agent.

Materials and Methods: The clinical records of patient Eyes with a history of RVO that were treated with IVR and had at least two years of follow-up were retrospectively analyzed. 40 eyes of 40 patients participated in this retrospective study; 20 eyes had branch RVOs (BRVOs), and 20 had central RVOs (CRVOs). Data from patients' medical records were examined, encompassing demographic information, duration of follow-up, and the evolution of best corrected visual acuity (BCVA) using ETDRS charts. The area of the foveal avascular zone (FAZ) was quantified using the initial angiogram that was accessible and the angiogram that was conducted during the last cross-sectional visit.

Results: The BRVO group comprised 14 males and 6 females, while the CRVO group comprised 8 males and 12 females. The average age of the patients in the BRVO group was 57.86 years, while in the CRVO group it was 62.32 years. The initial FAZ area (mm2) was 47.1 ± 26.0 in the CRVO group and 0.44 ± 0.31 in the BRVO group. The initial BCVA(L) was 51.8 ± 24.1 in the CRVO group and 47.1 ± 26.0 in the BRVO group. The final FAZ area (mm2) was 0.47 ± 0.21 in the ischemic CRVO, 0.32 ± 0.12 in the non-ischemia CRVO, 0.48 ± 0.34 in the ischaemic BRVO and 0.41 ± 0.21 in the non-ischaemic BRVO. The final BCVA (L) was 39.8 ± 16.8 in the ischemic CRVO group, 69.8 ± 18.1 in the non-ischemia CRVO group, 37.9 ± 17.6 in the ischaemic BRVO group, and 61.2 ± 21.2 in the non-ischaemic BRVO group, all statistically significant..

Conclusion: Ranibizumab was found satisfactory in the long-term treatment of macular edema secondary to RVO and was not associated with increased macular ischemia.

Keywords: Macular Edema, Retinal Vein Occlusion, Foveal Avascular Zone, Best Corrected Visual Acuity.

Introduction

Retinal vein occlusion (RVO) is the second most prevalent retinal vascular disease that causes vision loss [1]. It is typically classified into two types: central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO) [2].

Systemic comorbidities play an important role in the etiology of RVO [1, 3]. Increased production of vascular endothelial growth factor (VEGF) develops early in the disease phase and contributes significantly to macular edema [4-6]. Fundus fluorescein angiography (FFA) has long been accepted as the gold standard for diagnosing retinal vascular disorders, including RVO [7]. This approach includes injecting fluorescein dye intravenously and then taking consecutive photographs of the dye's circulation within the retinal vessels using a specialized camera [8]. FFA offers crucial information on the perfusion state, existence of vascular anomalies, and alterations in the foveal avascular zone (FAZ) associated with RVO [9, 10].

FFA-based RVO examination allows clinicians to visualize and assess the amount of retinal vascular involvement [11]. Venous blockage, regions of

non-perfusion, capillary leakage, and neovascularization can all be seen, which helps with the proper diagnosis and classification of RVO [12]. Furthermore, FFA enables the accurate assessment of FAZ changes, which are critical in predicting visual outcomes in patients with retinal vascular disorders [13].

FFA allows clinicians to study the FAZ area, which is the middle portion of the retina devoid of blood vessels. Changes in FAZ area, such as enlargement or irregularity, have been linked to RVO severity and prognosis [14-16]. These changes can represent the severity of retinal ischemia and provide information about the functional impairment reported by patients.

The study was conducted to assess the changes in foveal avascular area (FAZ) and visual gain in patients with macular edema caused by retinal vein occlusion (RVO) treated with intravitreal ranibizumab, an anti-VEGF drug.

Materials and Methods

A retrospective study was conducted in the department of Ophthalmology at Regional Eye Hospital, Visakhapatnam. Every participant provided signed informed consent, and the study was carried out with approval from the institutional ethics committee. The medical records of patients with RVO followed in our Department were reviewed.

If the patient had no history of uveitis, dense cataracts, vitreoretinal disease, or other conditions that would impair visual acuity (VA), then their eyes with a history of RVO treated with IVR were included in the study, with a minimum follow-up of two years. Additionally excluded were patients who had undergone scleral buckling surgery or had previously undergone a vitrectomy. Information from patients' medical records was examined, such as demographics, follow-up duration, evolution of best correct visual acuity (BCVA) using ETDRS charts, previous treatments for macular edema, neovascular disease development and panretinal photocoagulation treatment, other ocular comorbidities, intraocular surgery, and systemic or adverse effects associated with IVR treatment.

Retreatment was carried out during follow-up if the BCVA loss was greater than five Early Treatment of Diabetic Retinopathy Study (ETDRS) letters (L) or if intraretinal or subretinal fluid was seen in the OCT image. Every patient underwent a final cross-sectional assessment, which included the following: BCVA (ETDRS charts).

The foveal avascular zone (FAZ) area was measured in the first available angiogram and in the angiogram performed in the final cross-sectional visit. The software computed the area of two independent observers automatically for this purpose. The program uses a circular grid, calibrated through the margins of the optic disk and centered in the macula, to partition the posterior pole into ten subfields. This grid is identical to the macular grid used in ETDRS, which consists of 1-, 3-, and 6-mm concentric circles. The central macula and the central subfield overlap. In the last visit, more RNP regions were qualitatively examined for subtyping into ischemia and nonischemic groups. If the RNP region was more than 10 disk areas in eyes with CRVO or 5 disk areas in eyes with BRVO, it was deemed ischemic.

IBM SPSS Statistics version 21.0) was used for statistical analyses. P value less than 0.05 was regarded as statistically significant.

Results

The study involved 40 patients. 20 of the 40 patients were assigned to the BRVO group and another 20 to the CRBO group. Table 1 provides an overview of each patient's clinical features. In the BRVO group, there were 14 men and 6 women, while in the CRVO group, there were 8 men and 12 women. Patients with BRVO had an average age of 57.86 years, whereas those with CRVO had an average age of 62.32 years.

Table 1: Baseline clinical characteristics:

	CRVO (n=20)	BRVO (n=20)
Age (years)	57.86 ± 12.14	62.32 ± 12.25
Sex (males/females)	14/6	8/12
Initial FAZ area	0.41 ± 0.41	0.44 ± 0.31
Initial BCVA	51.8 ± 24.1	47.1 ± 26.0
Systemic diseases		
Hypertension	2	2
Diabetes mellitus	7	8
Dyslipidemia	5	6

The final visit revealed eight eyes (40%) in the CRVO group and seven eyes (35%) in the BRVO group to be ischemic. Differences between ischemic and non-ischemic eyes for the final FAZ area and BCVA are presented in table 2

Table 2: Final FAZ area and BCVA in ischemic and non-ischemic eyes in both groups

Parameter	CRVO			BRCO		
	ischaemic	Non-ischaemic	p value	ischaemic	Non-ischaemic	p value
Final FAZ area, mm^2	0.47 ± 0.21	0.32 ± 0.12	0.002*	0.48 ± 0.34	0.41 ± 0.21	0.002*
Final BCVA, L	39.8 ± 16.8	69.8 ± 18.1	0.001*	37.9 ± 17.6	61.2 ± 21.2	0.002*

*Significant

Discussion

Vein occlusion in RVO patients may induce high venous pressure, turbulent blood flow, and overloaded drainage capacity, resulting in dilatation of retinal veins and capillaries [17].

Simultaneously, the intraocular level of VEGF rises dramatically after vein blockage, and it is the most essential mediator of neovascularization and macular edema. Thus, VEGF inhibitors have been shown to be an effective first-line therapeutic method for addressing neovascularization and macular edema caused by RVO [18].

VA grew steadily in the first 6 months, as expected in both groups; however, the observed rise was lower than that reported in the BRAVO and CRUISE trials [19, 20].Acutely following BRVO or CRVO, RNP can be minimal or absent (nonischemic RVO), or severe (ischemic RVO). Measurements of the area of RNP on FA have revealed that enlargement is prevalent in both BRVO and CRVO [21, 22].

The mechanism is unknown, however concerns have been raised that it may be increased by VEGF itself [23] or, conversely, by its suppression [24, 25]. For this reason, we examined the changes in the FAZ area in eyes with RVO treated with IVR over time.

These differences, however, were minor and significant in both groups. The outcomes of our investigation do not corroborate the early worries about worsening retinal ischemia after prolonged therapy with ranibizumab.

Another significant observation was that ischemic eyes had larger final FAZ regions and a poorer functional outcome. This is consistent with the concept of the role of higher levels of VEGF in the progression of RNP, as well as the fact that, as stated by Sophie et al. [26], infrequent ranibizumab injections to control edema in patients with RVO may not be sufficient to prevent progression of RNP in all cases, potentially contributing to long-term loss of visual gains. It is also worth noting that in our trial, ranibizumab did not prevent retinal neovascularization or rubeosis.

This was also mentioned in a recent publication [27]. As a result, the effect of ranibizumab in preventing progression of ischemia and subsequent development of neovascular disease needs to be further studied.

Conclusion

It is concluded that ranibizumab was effective in the long-term treatment of macular edema due to RVO and was not linked with increased retinal ischemia.

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