



INTRAVITREAL BEVACIZUMAB AIDS REDUCTION OF MACULAR EDEMA DUE TO CENTRAL RETINAL VEIN OCCLUSION (CRVO)

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Abstract : AIM - We aimed to evaluate the role of intravitreal bevacizumab injection in reduction of macular edema and improvement of visual acuity in patients with CRVO. METHODS - Twenty eyes of 20 patients (fourteen males and six females) with CRVO received intravitreal bevacizumab 2.5 mg per 0.1ml. Twelve (60 percent) were hypertensive, eight (40 percent) were diabetics, and two (20 percent) had ischemic heart disease. The baseline visual acuity was more than 0.1 decimals in five (35 percent) patients, and worse than 0.1 decimals in fifteen (75 percent) patients. RESULTS - The mean baseline macular thickness decreased from 799 microns to 194 microns ('p' value less than 0.001). Mean visual acuity improved from 0.14 decimals preoperatively to 0.29 decimals after intervention ('p' value 0.006). The visual acuity at six months had improved to 0.33 decimals in six (30 percent) patients, 0.29 decimals to 0.1 decimals in eight (40 percent) patients, and less than 0.1 decimals in six (30 percent) patients. Three eyes developed iris neovascularization. CONCLUSION - Bevacizumab aids reduction of macular edema in CRVO and improves visual acuity.

Keyword : Bevacizumab, Central retinal vein occlusion, Macular edema

INTRODUCTION Central retinal vein occlusion (CRVO) is a condition characterized by dilation and tortuosity of the retinal venules with hemorrhages in all four quadrants of the retina. Often there is concomitant optic nerve swelling and macular edema, and there may be exudative detachment of the retina, neovascularization of the iris, and neovascular glaucoma. After diabetic retinopathy, CRVO is the second most common retinal vascular disease affecting the retina.^{1,2}

Intravitreal levels of vascular endothelial growth factor (VEGF) in CRVO are the highest of those measured in retinal vascular disease,³ and the severity of findings in CRVO is proportional to intravitreal VEGF levels.⁴ Almost all of the features of CRVO can be induced in primate eyes by intravitreal injection of VEGF, including vascular dilatation, tortuosity, intraretinal hemorrhage, and capillary nonperfusion.⁵ Intravitreal VEGF injections in primates cause little or no retinal neovascularization.⁵

Inhibiting VEGF would seem to be a rational strategy for treating CRVO. Intravitreal injection of anti-VEGF agents caused regression of iris neovascularization.^{6,7} CRVO was among the first diseases treated with intravitreal bevacizumab,⁸ and subsequent case series showed a large proportion of patients having visual acuity (VA) improvement.^{9,10} Bevacizumab treatment early after the onset of CRVO was associated with a statistically significant reduction in venous dilation, tortuosity, optic disc swelling, and macular edema in addition to improvement of VA.¹¹

We aimed to evaluate the role of intravitreal bevacizumab injection in reduction of macular edema and improvement of visual acuity in patients with CRVO.

METHODS

All patients presenting at retina clinic of our hospital with clinical diagnosis of CRVO between September 2010 and April 2011 were considered for inclusion criteria. Inclusion criteria were the administration of intravitreal bevacizumab injection within three months of onset of the venous occlusive event and follow-up period of at least six months, visual acuity less than 6/12 at presentation, central macular thickness more than 200µm, and patients with minimal or no lens changes. Exclusion criteria included the presence of co-existing retinal pathology affecting vision, increased intraocular pressure (IOP) due to neovascular glaucoma (NVG) at presentation, corneal or lens opacities, irregular follow-up. The intervention procedure was intravitreal bevacizumab injection in the dose of 2.5 mg/0.1 ml. Patients were followed at monthly intervals, and monitored by optical coherence tomography (OCT). Data from the ophthalmologic examination, including best-corrected visual acuity, biomicroscopy, color fundus photography, fluorescein angiography, and OCT, were recorded before and throughout the course of treatment. The main outcome measures were changes in visual acuity and central macular thickness edema.

RESULTS

Twenty eyes of 20 patients' fourteen males and six females with CRVO were included in the study. The mean age of the patients was 57.27 years. Twelve (60%) were hypertensive, eight (40%) were diabetics, and two (20%) had ischemic heart disease.

The baseline visual acuity was more than 6/60 in five (35%) patients, and worse than 6/60 fifteen (75%) patients, the mean baseline macular thickness was 799µm. The visual acuity at six months had improved to 6/18 in six (30%) patients, 6/24 to 6/60 in eight (40%) patients, and less than 6/60 in six (30%) patients. The macular thickness at six months had decreased to 194µm. The mean baseline visual acuity was 0.14 (Decimal visual acuity; approximately 6/60). At 6 months the mean visual acuity was 0.29 (Decimal visual acuity; approximately 6/24). This improvement was statistically significant (p=0.006). The mean baseline macular thickness was 799µm. At 6 months, the mean macular thickness was 194µm. There was a significant decrease in the macular thickness (p=0.001). There were no complications related to intravitreal injection and recurrence of macular edema during the follow-up period. Three eyes developed iris neovascularization.

DISCUSSION The prospective study showed that intravitreal bevacizumab given for CRVO within three months of onset was associated with improved visual acuity and decreased macular edema. However, the treated patients also had rapid clearance of retinal hemorrhages, decreased venous dilatation, and tortuosity all beginning quickly after intravitreal bevacizumab injection. The natural history of CRVO is well known and the functional and anatomic outcomes of our patients seemed to be better than those reported with alternative therapeutic approaches, although eligibility criteria differed among studies.^{12,13,14,15} In the CRVO study,¹⁴ patients were categorized by a number of variables, including a fluorescein angiographic classification of perfused eyes, nonperfused eyes, and eyes with indeterminate status,¹⁴ a classification that has been criticized for a number of reasons.^{9,15} Patients with extensive retinal hemorrhage could not be classified initially and were considered to be indeterminate.^{14,16} Most patients in indeterminate group eventually were classified as having a nonperfused status.

Patients with CRVO have the possibility of progressing to neovascularization of the iris which seemed to be common in patients determined as having ischemic disease and poor baseline vision.

In current study three patients developed neovascularization of the iris.

The improvement in multiple aspects of the induced abnormalities caused by CRVO resulted from the intravitreal injection. The visual acuity improved. The observed decrease in edema may be secondary to the reduction of vascular permeability caused by inhibiting VEGF, but the rapid reduction in retinal hemorrhages, and venous tortuosity cannot be explained directly by antipermeability effects. This marked decrease in the dilatation and tortuosity of the venous system implies the venous pressure must have been reduced substantially and quickly after bevacizumab injection.

The improvement of visual acuity after bevacizumab injection was concordant with decreased in central macular thickness. Hence regular OCT examinations are regarded helpful for early detection of an impending drop in visual acuity after bevacizumab injection. From the natural course of retinal vein occlusion, the imbalance between inflow and outflow of the retinal circulation can prevail for several months or even years. The formation of a new blood flow balance is supported by the formation of collateral disc vessels with a new drainage route.¹⁷

Decrease in visual acuity is mainly due to macular ischemia, cystoid macular edema and photoreceptor damage in the early period of the disease. Retinal vein occlusion treatment mainly aims at causal therapy for improved blood circulation; and prevention of secondary changes such as CME and neovascular complications. The positive effect of bevacizumab injection on central macular thickness and visual acuity is evident when mean values are considered. Bevacizumab acts by inhibits angiogenesis temporarily. Hence long term follow-ups are needed to assess the capability of Avastin to reduce macular ischemia of CRVO.

CONCLUSION

Bevacizumab aids reduction of macular edema and improves visual acuity in patients with central retinal vein occlusion. There is direct correlation between macular thickness reduction and visual acuity improvement.

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(Fig 1 a) Colour fundus photograph obtained at presentation showing retinal hemorrhage , venous dilatation and tortuosity , and macular edema consistent with CRVO.(Fig 1 b) OCT image showing macular edema with the central macular thickness of 682 μ m. (Fig 1 c) After six months post treatment shows near normal retinal appearance. (Fig 1 d) Post-treatment OCT image shows reduction of central macular thickness to 182 μ m.

figure 1a



Figure 1b

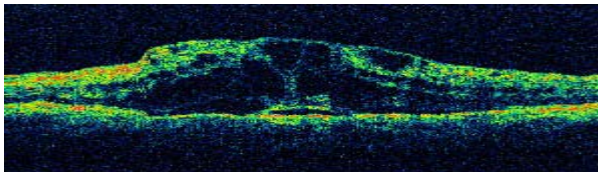


figure 1c

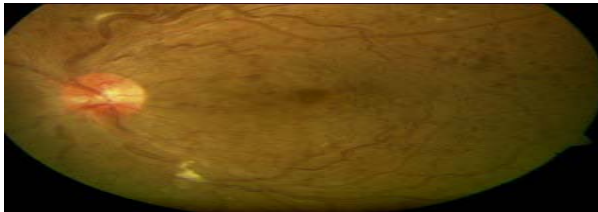


figure 1d

