CLINICAL INVESTIGATION

Visual Acuity Following Intravitreal Bevacizumab for Macular Edema Associated with Retinal Vein Occlusion

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Abstract

Purpose: To study prognostic factors for visual acuity (VA) after intravitreal bevacizumab injection (IVB) for macular edema (ME) associated with retinal vein occlusion (RVO), by evaluating the correlation between the final VA and VA at baseline and at 1, 3, and 6 months after the initial IVB.

Methods: We studied retrospectively 79 eyes of 79 patients with ME secondary to RVO treated with IVB. The correlation between the final VA and VA at each visit was studied by using Pearson's correlation coefficient.

Results: Baseline VA was significantly correlated with the final VA ($r = 0.552, P < 0.0001$). Postoperative VA at 1, 3, and 6 months after the initial IVB, however, was even more closely correlated with the final VA ($r = 0.793, 0.816, 0.893$, respectively; $P < 0.0001$ in each case). Additionally, eyes with a VA of 20/40 or better at 1 month achieved a significantly better final VA than did eyes with a VA worse than 20/40 at 1 month ($P < 0.0001$). This tendency was seen also in each RVO subgroup.

Conclusion: Although the baseline VA was significantly correlated with the final VA, postoperative VA was correlated even more closely with the final VA. VA shortly after the initial IVB seemed to reliably predict final visual outcome.

Keywords: bevacizumab, macular edema, photoreceptor layer, retinal vein occlusion, visual acuity

Introduction

Macular edema (ME) is a major vision-threatening complication associated with retinal vein occlusion (RVO). In RVO, increased intravascular pressure and reduced blood flow in the macular capillaries lead to dysfunction of the endothelial blood–retinal barrier and to increased vascular permeability, resulting in ME. Vascular endothelial growth factor (VEGF) may play an important role in the pathogenesis of ME secondary to RVO. Although grid laser photocoagulation is the only evidence-based effective treatment for ME secondary to branch retinal vein occlusion (BRVO), visual recovery is both slow and limited. In addition, there is no established treatment for visual acuity (VA) decrease due to ME secondary to central retinal vein occlusion (CRVO).

Anti-VEGF therapy is a specific and widely used treatment for ME associated with RVO. Since Rosenfeld et al. first reported the efficacy of intravitreal bevacizumab (IVB) (Avastin, Genentech, South San Francisco, CA, USA) for ME secondary to CRVO, a number of case series have shown it to have promising short-term effects, with immediate reduction in foveal thickness and improvement in VA. More recently, the efficacy of ranibizumab (Lucentis, Genentech) for ME secondary to RVO has been reported. However, although anti-VEGF therapy is simple for the
treatment of ME secondary to RVO, a major drawback of this treatment is a high reported rate of ME recurrence, with a concomitant decrease in VA.

In the clinical setting, IVB does indeed show remarkable short-term effects on ME associated with RVO. Shortly after IVB treatment, ME often regresses to physiological levels, accompanied by an improvement in VA. However, the visual prognosis of these eyes varies. Some eyes maintain the improvement in VA with no recurrence of ME. Most eyes, however, subsequently show recurrent ME, often accompanied by a decrease in VA. The final VA seems to depend on various factors, such as the final condition of the foveal photoreceptor layer, the presence of the foveal deposition of hard exudates, and the initial severity of the ischemia.

To date, baseline VA has been thought to be one of the most reliable prognostic factors of visual prognosis in patients with RVO. Chung et al. reported that eyes with BRVO that show an improvement in VA at 1 month after IVB often have good final visual recovery. However, limited information is available on the visual prognosis of eyes with ME secondary to RVO that had been treated with anti-VEGF therapy. In the current study, we examined VA at baseline and at 1, 3, and 6 months after the initial IVB for the treatment of ME secondary to RVO, and investigated the correlation between VA at each visit and the final VA in order to better assess factors involved in the visual prognosis of patients with decreased VA due to ME associated with RVO.

**Subjects and Methods**

**Patient Selection**

For this retrospective study, we reviewed the medical records of 104 patients (105 eyes) who had received IVB as treatment for visual disturbance resulting from ME associated with RVO. They received the initial IVB between October 2006 and December 2007 and were followed up for at least 12 months after the initial IVB at Kyoto University Hospital. Of the 105 eyes, 26 were not included in the study because of one of the following exclusion criteria: a history of vitreous surgery, treatment with intravitreal or sub-Tenon triamcinolone acetonide within 3 months or with grid laser photocoagulation within 6 months, or a coexisting ocular disease (i.e., epiretinal membrane, glaucoma, proliferative diabetic retinopathy, or senile cataract causing decreased VA). Pseudophakic eyes were included. As a result, 79 eyes of 79 patients were included in the study. Of these 79 eyes, 42 had BRVO, 13 had hemi-CRVO, and 24 had CRVO. The study was approved by the Institutional Review Board of Kyoto University Graduate School of Medicine and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from each patient.

All patients had undergone a comprehensive ophthalmologic examination, including best-corrected VA measurement, slit-lamp biomicroscopy, indirect fundus ophthalmoscopy, fluorescein angiography (FA), and optical coherence tomography (OCT) examinations. Best-corrected VA was measured with a Landolt chart and converted into the logarithm of the minimal angle of resolution (logMAR). At the initial visit, all patients underwent FA using a confocal laser scanning system (HRA-2, Heidelberg Engineering, Heidelberg, Germany) except those with a high risk of allergy to sodium fluorescein solution. An OCT examination was performed in all patients to evaluate the effectiveness of the treatments for ME and to measure the foveal thickness at each visit. In this study, the ophthalmologic data obtained at baseline and at 1, 3, and 6 months after the initial IVB and that obtained at the final visit were used.

**Intravitreal Bevacizumab Injection**

In the current study, 79 eyes of 79 patients with decreased VA due to ME associated with RVO were treated with IVB. The mean duration of symptoms before IVB ranged from 1 to 46 months (6.6 ± 8.6 months). Of the 79 eyes, 31 (39%) received the initial IVB within 3 months from the onset of symptoms. The dosage of bevacizumab was 1.25 mg/0.05 ml per injection, and all injections were performed in the usual sterile fashion; prophylactic topical antibiotics were applied for 1 week after the injection. No local or general adverse events associated with IVB occurred. Each patient was scheduled to visit our clinic for an examination at a 1- to 2-month intervals.

ME was judged to be resolved completely when the foveal thickness was reduced to <250μm and when no cystoid spaces were seen in the foveal region. Recurrence of ME was defined as a rebound in foveal thickness to >300μm or the presence of intraretinal cystoid spaces in the foveal region after the ME was resolved by IVB. Re-injection of bevacizumab was performed if the eye showed a recurrence of ME with a decrease in VA, provided the patient agreed to retreatment.

**Correlations in VA**

Baseline VA and VA at 1, 3, and 6 months after the initial IVB and final VA were recorded and assessed. Correlations of VA were investigated using Pearson’s correlation coefficient. In addition, on the basis of the VA at 1 month we divided the study eyes into two groups, those with VA equal to or better than 20/40 and those with VA worse than 20/40, and investigated whether the final VA in the two groups was significantly different. These analyses were performed for all 79 eyes, both eyes in each group classified by the final ME condition (resolved or not), and eyes in each group classified by the type of RVO (BRVO, hemi-CRVO, or CRVO).

**OCT Measurement**

In all patients, an OCT examination was performed to measure the foveal thickness, primarily with the Stratus OCT or Cirrus HD-OCT (Carl Zeiss, Dublin, CA, USA) or,