

Intravitreal Bevacizumab Promising for Neovascularization in Diabetic Retinopathy

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A single injection of intravitreal bevacizumab (Avastin; Genentech, San Francisco) was associated with rapid regression of persistent neovascularization in diabetic retinopathy—refractory to panretinal laser photocoagulation (PRP)—as well as visual acuity improvement for at least 12 weeks.¹ We published our results in *Retina*.

While fluorescein angiographic evaluation suggests that the drug-induced effects on neovascularization are transient, anti-vascular endothelial growth factor (VEGF) therapy using intravitreal bevacizumab may control this vision-threatening condition at least temporarily and, consequently, delay or prevent its main complications (vitreous hemorrhage and tractional retinal detachment).

Among patients with diabetes, retinal neovascularization is an important risk factor for severe vision loss. About 60% of patients with proliferative diabetic retinopathy respond to scatter laser treatment with neovascularization regression within 3 months. Many patients, however, require additional laser treatments and 4.5% require pars plana vitrectomy. While PRP can prevent severe central vision loss associated with proliferative diabetic retinopathy, it is destructive, expensive, and very often painful. Patients also experience a decrease in peripheral vision.

VEGF BACKGROUND

VEGF has been implicated in human eye disease characterized by neovascularization. Blockage of VEGF has been associated with the inhibition of iris neovascularization and suppression of retinal new vessel formation

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in primates. This is the basis for the rationale for anti-VEGF therapy in retinal vascular diseases associated with new vessel formation.

There are several clinical trials underway evaluating the role of anti-VEGF agents for the treatment of ocular disease associated with choroidal and/or retinal neovascularization and exudative processes. Promising anecdotal reports of bevacizumab in patients with choroidal neovascularization, macular edema, vitreous hemorrhage, and iris neovascularization led us to our current investigation of this off-label indication.

EVALUATION OF SINGLE 1.5-MG DOSE

We evaluated the short-term fluorescein angiographic and visual acuity effects of a single 1.5-mg bevacizumab dose in a prospective, nonrandomized, open-label study of patients with diabetes who had active leaking refractory to laser treatment. Patients also had Early Treatment Diabetic Retinopathy Study (ETDRS) BCVA <20/40. We performed a standardized ophthalmic evaluation at baseline and again following intravitreal bevacizumab administration at weeks 1, 6, and 12.

There were 15 consecutive patients included (nine

men), with a mean \pm SD age of 60.08 ± 7.75 years.

At baseline, the patients had a mean \pm standard error of the mean (SEM) neovascular leakage area of 27.79 ± 6.29 mm². The mean \pm SEM area of active leaking neovascularization decreased significantly to 5.43 ± 2.18 mm² and 5.50 ± 1.24 mm² ($P < .05$, Tukey multiple comparisons posttest) at 1 and 12 weeks postinjection, respectively.

The mean \pm SEM logMAR (Snellen equivalent) BCVA improved significantly from 0.90 or 20/160 ± 0.11 at baseline to 0.76 or 20/125+2 ± 0.12 , 0.77 or 20/125+2 ± 0.11 , and 0.77 or 20/125+2 ± 0.12 at weeks 1, 6, and 12, respectively ($P < .05$ Tukey multiple comparisons posttest).

No major adverse events associated with treatment were observed.

Further studies are needed to evaluate the safety and efficacy of intravitreal bevacizumab.

MORE INVESTIGATION WARRANTED

Of the scheduled follow-up intervals in the study, the maximum drug-related effects were evident at week 6, when complete absence of leakage from neovascularization noted at baseline was demonstrated in all patients. Not surprisingly, the recurrence of neovascular leakage was observed in 14 of the 15 eyes at week 12.

Whether the short-term effects of bevacizumab treatment may be sustained with additional injections remains to be determined. Further studies are also needed to evaluate the safety and efficacy of intravitreal bevacizumab, the potential value of repeated injections and the optimal injection frequency, as well as to compare it with other treatment modalities. ■

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1. Jorge R, Costa AR, Calucci D, et al. Intravitreal bevacizumab (Avastin) for persistent new vessels in diabetic retinopathy (IBEPE Study). *Retina*. 2006;26:1006-10013.

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