Intravitreal Bevacizumab for Vitreous Hemorrhage Secondary to PDR

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Proliferative diabetic retinopathy (PDR) is the leading cause of blindness in individuals aged 20 to 65 years old.[1,2] In PDR, various angiogenic factors, including VEGF, are responsible for neovascularization, fibrovascular proliferation, vitreous hemorrhage, and retinal detachment.[1,3-6] Vitreous hemorrhage is 1 complication of PDR and a major cause of vision loss.[7]

Laser photocoagulation has been the gold standard for treatment of PDR.[3,4] However, it can be difficult or impossible to perform in patients with cataracts or vitreous hemorrhage. Bevacizumab (Avastin, Genentech) is a humanized recombinant antibody that binds all isoforms of VEGF.[4,8] In 2006, Spaide and Fisher described the use of intravitreal bevacizumab for vitreous hemorrhage in 2 patients with PDR, noting a decline of neovascularization and resolution of vitreous hemorrhage with an improvement of 2 to 5 lines of visual acuity after 1 month of treatment.[9,10] This article presents a study we conducted in a series of 73 patients with vitreous hemorrhage secondary to PDR and no retinal detachment who were treated with intravitreal bevacizumab.

METHODS

This study included 89 eyes of 73 patients with vitreous hemorrhage due to PDR between January 2010 and June 2010. Patients with retinal detachment were excluded. Patients were assigned to 1 of 4 groups (Table 1) according to vitreous hemorrhage classification (Tables 1 and 2). A single dose of 1.25 mg intravitreal bevacizumab was administered.

Follow-up was performed at 1 and 6 weeks after injection. Resolution criteria for vitreous hemorrhage were:

1. Complete improvement: Complete resolution or fundus visible over 90% of total area
2. Partial improvement: Partial resolution compared with previous exam and fundus visible in less than 90% of total area
3. No improvement: Patients without improvement or with worsening

TABLE 1. PATIENT CLASSIFICATION OF VITREOUS HEMORRHAGE

Group 1	Group 2	Group 3	Group 4
Vitreous hemorrhage (+), (++) less than 3 months	Vitreous hemorrhage (+++), (++++) less than 3 months	Vitreous hemorrhage (+), (++) more than 3 months	Vitreous hemorrhage (+++), (++++) more than 3 months

TABLE 2. VITREOUS HEMORRHAGE SEVERITY

Vitreous Hemorrhage (+)	Vitreous Hemorrhage (++)	Vitreous Hemorrhage (+++)	Vitreous Hemorrhage (++++)
Details can be seen in fundus	Papillary silhouette and arcades can be seen, without details of fundus	Papillary silhouette is the only structure visualized	No details can be seen

TABLE 3. STUDY PARTICIPANTS				
	Eyes (patients)	Age (median)	% Women	Complications
Group 1	30 (25)	63	32%	0%
Group 2	25 (24)	57	50%	0%
Group 3	18 (13)	55	46%	0%
Group 4	16 (11)	60	55%	0%
Total	89 (73)	59	46%	0%

RESULTS

Results are shown in Table 3 and Figures 1 and 2. Group 1 comprised 30 eyes (25 patients), group 2 comprised 25 eyes (24 patients), group 3 comprised 18 eyes (13 patients), and group 4 comprised 16 eyes (11 patients). More than half of eyes presenting with mild and moderate vitreous hemorrhage and patients with severe vitreous hemorrhage less than 3 months responded favorably after bevacizumab injection, while nearly 70% of eyes with severe, long-standing vitreous hemorrhage did not respond.

DISCUSSION

PDR is a significant cause of blindness in working-age individuals.[6] Until recently, waiting for the hemorrhage to spontaneously resolve or performing pars plana vitrectomy were the only lines of treatment for vitreous hemorrhage due to this condition. Previous studies have analyzed the effects of intravitreal bevacizumab for the treatment of PDR complicated with vitreous hemorrhage, showing improvement of visual acuity from the first week of application. Despite limited follow-up, repeated intravitreal injections appear to be safe and well tolerated.[4,10,11]

In 2006, Spaide first reported improvement of PDR-related vitreous hemorrhage in 2 patients after injection of intravitreal bevacizumab. In both patients, there were improvements in visual acuity, and vitreous hemorrhage was partially resolved from the first week of application. Second doses were required by 1 patient after 1 month and by the other after 3 months. Reduction in neovascularization and retinal reperfusion were demonstrated by fluorescein angiography 1 month after the injection.[10]

Batarny and colleagues[4] reported visual and anatomic results in 10 patients presenting with PDR and vitreous hemorrhage that were treated with 1.25 mg of intravitreal bevacizumab. In their series, complete improvement of vitreous was seen in 4 eyes and residual hemorrhage in 2 eyes. Regression of neovascularization was observed in 7 eyes. These changes were evident 2 weeks after the injection.

Moradian et al[12] evaluated 38 patients with PDR and vitreous hemorrhage. One to 3 injections of 1.25 mg bevacizumab were administered in at 6- to 12-week intervals. Results showed vitreous hemorrhage improvement, fibrovascular tissue regression, and visual acuity gain from the first

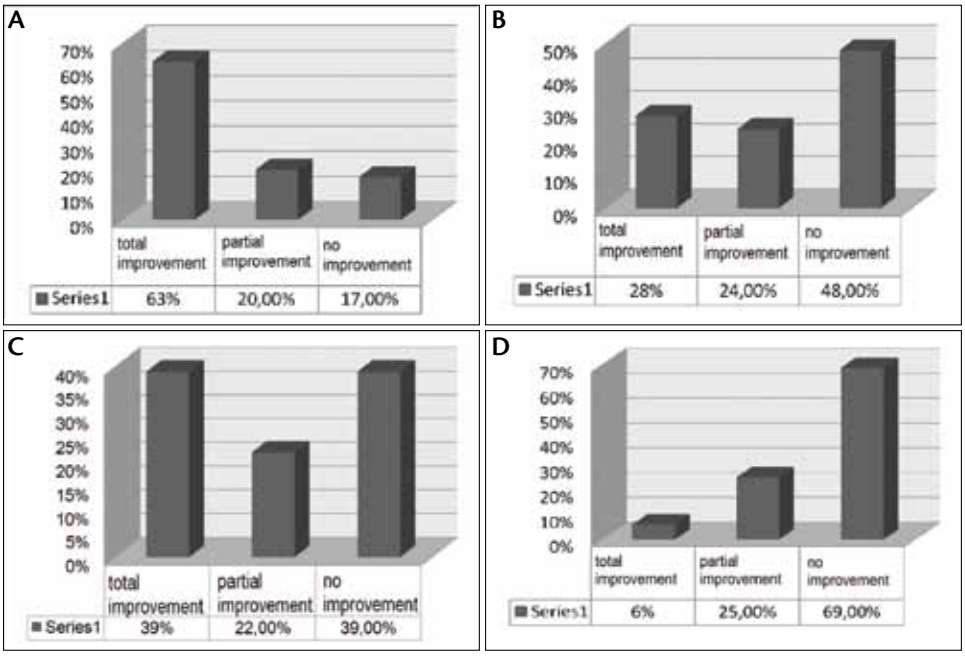

Figure 1. Vitreous hemorrhage improvement in group 1 (A), group 2 (B), group 3 (C), and group 4 (D) following intravitreal injection of bevacizumab.

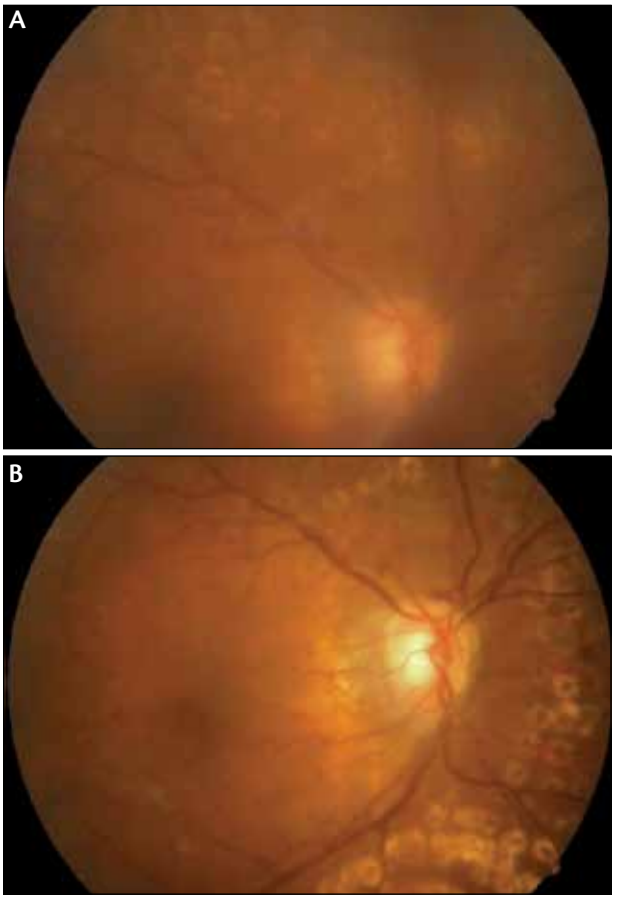

Figure 2. Patient with vitreous hemorrhage (++) of less than 3 months (A). Six weeks after 1.25 mg intravitreal bevacizumab injection, the vitreous hemorrhage is completely resolved (B).

week of treatment. Two cases developed fibrous contraction leading to retinal detachment.

Huang and colleagues[9] reported a series of 40 patients with vitreous hemorrhage due to PDR who received 1.25 mg of bevacizumab. Thirty-one eyes showed vitreous hemorrhage regression after 2 weeks. A second injection was administered after 4 to 6 weeks. The study authors concluded that 1 or 2 doses of bevacizumab induced rapid improvement of vitreous hemorrhage and reduced the need for vitrectomy.

In all of these studies, the only reported complication was traction retinal detachment in patients with moderate fibrous proliferation that worsened after bevacizumab injection.[12,13]

CONCLUSION

To the best of our knowledge, ours is the first study that differentiates among patients regarding their vitreous hemorrhage characteristics, showing which have the greatest chance of improvement. Our results demonstrate that intravitreal bevacizumab produces partial or complete resolution of vitreous hemorrhage in patients with PDR, that it is especially useful in hemorrhages of recent onset, and that it can be a fine alternative to observation or surgery. Pars plana vitrectomy remains the first line of treatment for vitreous hemorrhage older than 3 months and for cases associated with fibrovascular proliferation and retinal detachment. Comparative studies with longer follow-up are required to define long-term outcomes and to identify possible dose-related complications. ■

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