

Treatment of Retinal Vein Occlusion

Individualized therapy is crucial to good patient outcomes.

BY GAURAV K. SHAH, MD

Retinal vein occlusion (RVO) is a restriction of the flow of blood leaving the retina. The resulting pressure can cause fluid and blood to leak, resulting in macular edema, macular ischemia, or neovascularization that can lead to vitreous hemorrhage and retinal detachment.

The most common reason for loss of vision is macular edema, and for patients who have macular edema secondary to RVO our treatment options include observation, laser, anti-vascular endothelial growth factor (anti-VEGF) therapy, and bolus intravitreal or sustained-release steroids. Our treatment is guided by past trials in this area. The Branch Vein Occlusion Study (BVOS) showed that laser photocoagulation can significantly lessen the development of neovascularization and the occurrence of vitreous hemorrhage in a patient with branch retinal vein occlusion (BRVO).¹ The Central Vein Occlusion Study (CVOS) did not show that laser treatment was beneficial in patients with central retinal vein occlusion (CRVO).² The Standard Care vs Corticosteroid for Retinal Vein Occlusion (SCORE) Study found that for BRVO³ laser treatment is preferred to an injection of intravitreal triamcinolone (IVTA) because it is safer and as effective, but that for CRVO the previous standard treatment of observation should be replaced with an IVTA injection.⁴ A phase 3, multicenter, randomized, sham injection-controlled study of the efficacy and safety of ranibizumab injection compared with sham in patients with macular edema secondary to BRVO (BRAVO) and a phase 3, multicenter, randomized, sham injection-controlled study of the efficacy and safety of ranibizumab injection compared with sham in patients with macular edema secondary to CRVO (CRUISE) showed that injections of ranibizumab are effective treatments for BRVO and CRVO, respectively.^{5,6}

DECIDING HOW TO TREAT

Part of the decision of how to treat RVO depends on whether a patient has CRVO or BRVO. McIntosh et al⁷ describe the natural history of CRVO as presenting with poor visual acuity (<20/40) that worsens over time. They

found that up to 34% of nonischemic CRVO converted to ischemic CRVO over a 3-year period. I consider CRVO worse than BRVO because it affects a greater area of the retina, so for CRVO I proceed more aggressively.

My approach also depends on the type of disease that I am treating. For a patient with ischemic CRVO, I am fairly aggressive in my approach, using anti-VEGF agents and steroids in combination for those patients, and possibly laser therapy for areas of ischemia. Because most cases of ischemic CRVO do not improve without treatment, by treating I am trying to decrease the risk of neovascularization of the iris and glaucoma.

For BRVO, I observe in order to allow spontaneous resolution. If BRVO does not resolve, I initiate therapy. I typically start with anti-VEGF therapy, either ranibizumab (Lucentis, Genentech) or bevacizumab (Avastin, Genentech). It is not yet known which is better for RVO, but we will soon begin enrolling patients in a new study, Bevacizumab Versus Ranibizumab in Treatment of Macular Edema From Vein Occlusion (CRAVE), which will compare the 2 compounds in a randomized fashion. I initially treat the patient with at least 2 injections of anti-VEGF therapy, and if the patient responds I continue that treatment. If the patient does not respond or has a suboptimal response, meaning vision does not improve and/or fluid is seen on optical coherence tomography (OCT), then I consider using steroids. It is important to obtain a fluorescein angiogram for nonresponders because some of these patients may have ischemia that is causing macular edema. For these patients I often use supplemental thermal laser.

CUSTOMIZED TREATMENT

It is likely that, as we gain more experience treating RVO with the expanded range of therapies, we will find that few or no treatments are standalone. The choices of treatment include laser, anti-VEGF agents, and steroids, and it is important to use the therapy that is most effective for each individual, often in combination with one another.

It should be noted that if therapy is applied and does not produce the desired response, this does not mean that therapy should be completely abandoned for a particular patient. Rather, it is a reasonable strategy to switch to another mode of treatment or to a combination approach. For example, if a patient is treated with an anti-VEGF agent and the response is less than satisfactory, the therapy may be switched to steroids. If some fluid persists, it may be effective to reapply anti-VEGF therapy. It is important to remember that, in a different setting, the initial treatment may be effective.

When choosing a steroid, I consider the patient's history. In a patient with intraocular pressure (IOP) issues, a history of glaucoma, or who is taking medicine for glaucoma, I will use a steroid in an extended-release delivery mechanism that is less likely to raise IOP, such as the dexamethasone intravitreal implant (Ozurdex, Allergan, Inc.). If they do not have any issues of glaucoma or IOP, and they have not had problems in the past, then I may administer an intravitreal injection of triamcinolone acetonide (Kenalog, Bristol-Myers Squibb). There are certain high-risk groups, particularly black patients, who have other vasculopathic factors and therefore may be at increased risk of having IOP elevation after intravitreal triamcinolone acetonide injection.

VITRECTOMY

Most patients, after receiving a combination of therapies including laser, anti-VEGF agent, and steroids, will have some level of response. The question then is whether that response is acceptable or suboptimal. In patients who are not satisfied with the results, surgery may be an option. If a patient has vitreous traction that may be causing macular edema, for example, I may decide to perform vitrectomy and internal limiting membrane (ILM) removal. However, I save the option of surgery until after I have applied medical therapy because subsequent anti-VEGF and intravitreal steroid injections will not work as well in that eye due to faster drug clearance after vitrectomy. For patients who have undergone a previous vitrectomy and who have RVO with macular edema, the best option will most likely be the dexamethasone intravitreal implant because of its durability.

COMPLICATIONS

Complications of any intravitreal injection can include iris neovascularization and vitreous hemorrhage, which can be managed with laser photocoagulation. The long-term use of steroids can result in cataract formation, so it is important to advise patients of this so that they can weigh the risks against the benefits of treatment. The most significant concerns with any use of a steroid are IOP spikes and glaucoma, and so for patients who are at risk

steroids should be avoided. For those who are candidates for either bolus injection or the sustained-release implant, informed consent is important. Most cases of IOP elevation with the dexamethasone intravitreal implant can be managed with topical glaucoma drops.

LOOKING AHEAD

The CRAVE trial will hopefully provide answers as to the comparative efficacy and safety of ranibizumab vs bevacizumab in the setting of newly diagnosed RVO. More information regarding CRAVE enrollment criteria and contact information can be found on the Web at: <http://1.usa.gov/v5KMqg>. Additionally, results from the phase 3 COPERNICUS study evaluating aflibercept (Eylea, Regeneron) for CRVO have been released, demonstrating significant gains in vision at 6 months with aflibercept vs sham.⁸

As our treatment armamentarium for RVO expands, it will be crucial to use the tools, both medical and surgical, that we have at our disposal to individualize therapy. As we are learning, patients respond differently to treatments, and the response also appears to be dependent upon when in the disease state treatments are applied. ■

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