

Retinal Vein Occlusion Management Updated Recommendations

Incidence of **retinal vein occlusion (RVO)** has been on the increase and a recent study has revealed that about sixteen million people worldwide have retinal vein occlusion and is the second only to diabetic retinopathy in producing blindness due to retinal vascular diseases.

Macular edema is the frequent cause of visual acuity loss in both **central retinal vein occlusion (CRVO)** and **branch retinal vein occlusion (BRVO)**, the later being more common (80%).

BRVO occurs at the arterio-venous (AV) crossing where-in the common adventitious sheath compression of the vein by the thickened arterial wall results in the vascular flow embarrassment, thrombus formation and occlusion.

CRVO occurs at or behind the lamina cribrosa where again the hardened artery in the common sheath presses on the vein to cause occlusion in the same way.

Important risks factors in RVO are high blood pressure, diabetes, glaucoma and age.

Branch Vein Occlusion Study (BVOS) found that BRVO is self limiting in about one third of the cases and the recommendations are to observe them for three months and if there is no improvement by this time then light grid pattern laser spots should be applied to the affected area of the retina. This treatment showed improvement of about 2 lines in visual acuity compared to untreated controls.

Central vein occlusion study (CVOS) found that CRVO is relatively asymptomatic; visual acuity reduction due to macular edema is comparatively lesser than BRVO. Central retinal vein occlusion is categorized as non ischemic, ischemic and intermediate and observed that there is no proven treatment of CRVO. In these cases laser application, though reduced macular edema, but did not improve visual acuity and hence recommended control of causative factors with observation until natural resolution. In marked peripheral non perfusion cases panretinal

photocoagulation (PRP) may be required to prevent neovascularization and rubeotic glaucoma.

In younger age CRVO cases there may be clotting abnormalities due to various disorders hence they should be examined by hematologist, advised and managed accordingly with aspirin etc.

With increasing incidence of main risk factors i.e hypertension and diabetes there is noticeable increase of RVO cases. There has also been an acute awareness that RVO management is not being adequately met and there is an urgent need for testing alternative and more effective modes of therapies besides mere observation and laser treatment recommended by BVOS (since 1984) and CVOS (since 1995).

Recently observations and recommendations of three new trials have been released.

1. **SCORE** (Standard care versus corticosteroids for retinal vein occlusion).
2. **BRAVO** (A study of efficacy and safety of Ranibizumab (Lucentis) injections in patients with macular edema secondary to BRVO),
3. **CRUISE** (A study of efficacy and safety of Ranibizumab (Lucentis) injections in patients with macular edema secondary to CRVO).

In SCORE trial steroids in the form of triamcinolone acetonide 1 mg and 4 mg and slow release dexamethasone implants were tried and compared with laser application. Due to steroid side effects like cataract and glaucoma and keeping the risk benefit ratio into consideration, grid laser application was preferred over steroids in BRVO

In CRVO low dose of steroids (1mg) was preferred over laser. Despite low steroid dose (1mg) patients were kept under observation for any requirement of IOP lowering drops.

BRAVO and CRUISE trials

Use of anti VEGF agents like Ranibizumab (Lucentis) resulted in the decrease of macular edema secondary

to BRVO and CRVO and was associated with significant visual acuity gains.

The effect became evident soon after first injection.

It was further observed that patients treated with Ranibizumab (Lucentis) alone were approximately three times more likely to be three-line gainers at 6 months than in sham group.

Which anti VEGF agent?

Despite Bevacizumab (Avastin) being off label drug and Ranibizumab (Lucentis) being projected to be superior to Bevacizumab (Avastin) in formulation, majority of the ophthalmologists prefer Avastin over lucentis; being nearly of equal efficacy and much less cost.

What Dose?

Various doses have been tried without very significant benefit of higher dose (Avastin 1.25mg and Lucentis 0.5mg)

What Protocol?

In RVO VEGF production is on going with resultant macular edema and neovascularization eventually and to counter it anti VEGF injections are recommended at about monthly intervals currently till we develop more effective and longer lasting modalities.

How Long?

Start the treatment with immediate injection and then monthly injections till the situation is stabilized and then if need be give injections with treat and extend protocol (tapering treatment) by assessing visual acuity and macular edema (with OCT) or resort to treating on as needed basis.

Role of Laser

Role of laser is important in RVO as there is some element of more or less ischemia in nearly all cases with the tendency of neovascularization in the long run if anti VEGF is not given indefinitely.

Patients with marked peripheral non perfusion should be kept under close observation or preferably PRP should be done in time.

When combining anti VEGF with laser, the protocol should be anti VEGF injection and after one

week, once edema is reduced, laser application is carried out.

Edema in RVO is predominantly at superficial level in the inner retinal layers due to production of VEGF by the ischemia of the photoreceptors and the aim of laser treatment is to apply it at the pigment epithelium layer level to cause ablation of photoreceptors to reduce VEGF production.

If there are retinal hemorrhages in RVO, the laser energy is absorbed by the blood in the superficial inner retinal layers destroying the nerve fiber layer causing damage rather than the required benefit of reducing VEGF production by ablating photoreceptors.

Hence laser should be avoided in the presence of retinal hemorrhages till these clear with the passage of time or with anti VEGF injections.

When grid laser application is contemplated for macular edema it should be applied judiciously because it causes permanent ablation which cannot be retraced, hence in cases where macular edema is controlled with anti VEGF or steroids, laser application maybe held off.

Risk Factors

Important recommendations are to attend to the risk factors in RVO like hypertension, cardiovascular diseases, diabetes, obesity and glaucoma.

Combination therapy

May be considered in resistant situation with anti VEGF, laser and steroids (maybe deep sub tenon injection of triamcinolone acetonide)

Caution

Be wary of the complications of repeated intravitreal injections like endophthalmitis, retinal detachment, retinal hemorrhages, and lens damage. Take precautions with proper aseptic protocol and timely detection and management if it happens.

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