Branch retinal vein occlusion (BRVO) is a cause of low vision among significant number of patients in this era of patients with multiple metabolic and cardiovascular ailments. Classical teaching mentions that it affects elderly age group (>60 years) with no gender predominance. However, more number of cases are being diagnosed at younger ages because of changing life styles. In India, inflammatory vein occlusions also contribute to significant number of cases.

Multiple treatments have been described for BRVO. Among them, anticoagulation therapy, arteriovenous sheathotomy, laser chorio-retinal anastamosis, hemodilution and other systemic therapies were not widely accepted as routine treatment options.

After BVOS (Branch Vein Occlusion Study) published in 1984, there was no major advancement in its management till recent years. Now, with the advent of anti – VEGF agents and intra- or peri-ocular steroid therapy, it appears that the BVOS lost its importance in last 2-3 years. Nonetheless, it is still valid and remains so as it is the only well designed and randomized clinical trial till date regarding management of BRVO. Also, the untreated group of BVOS gave insight into natural course of the disease.

This article aims to discuss current trends and acceptable protocols of management of BRVO.

**Etiopathology**

Risk factors: Systemic Hypertension, Diabetes Mellitus, Age more than 60 years, Glaucoma, Hemodynamic or thromboembolic disease, Retinal Vasculitis of any cause.

Atherosclerosis and thrombus formation at arterio-venous crossings of branch retinal vessels is the pathology responsible for BRVO associated with systemic metabolic disease. Occlusion can occur away from AV crossings in cases of retinal vasculitis.

Involvement of superotemporal vein appears to be most common as macula is affected and patients become symptomatic early. Involvement of veins away from macula gets diagnosed only during routine fundus examination or, more commonly, after vision loss due to vitreous hemorrhage.

In interim to late stages, compensated vein occlusion with development of collateral circulation does not require any active intervention except for regular follow-up.

**Figure 1:** Superotemporal BRVO
Uncompensated vein occlusion results in recurrent or chronic macular edema and neovascularization and further complications. Intraocular neovascularization supposedly occurs with retinal capillary non perfusion area of more than 5 disc diameters.

**Symptoms**

**Sudden diminution of vision**

BRVO involving macula: macular ischemia, macular edema (CME), hemorrhage at fovea

BRVO away from macula: Vitreous hemorrhage (VH), Tractional or combined tractional-rhegmatogenous retinal detachment (TRD or CRD)

**Horizontal field defect**

Early symptom; along with low vision if macula also involved

**Floaters**

Vitreous hemorrhage, inflammatory vein occlusion

**Asymptomatic**

Vein occlusion seen on routine clinical examination

**Signs**

**Early**

Moderate to severe vision loss, multiple dot and blot retinal hemorrhages and cotton wool spots in the area of involved vein with or without macular edema.

**Interim**

*Compensated vein occlusion:* Vision >6/12, Sclerosed retinal vein, Insignificant macular edema, Disc collaterals

*Uncompensated vein occlusion:* Vision <6/18, macular edema, retinal neovascularization (NVE), Disc neovascularization (NVD)

**Late (uncompensated)**

Severe vision loss (<6/60), chronic macular edema, vitreous hemorrhage, TRD or CRD, iris neovascularization (NVI), increased IOP

**Systemic Investigations**

*All patients:* Even in a known hypertensive or patient with other known systemic risk factor, following investigations
are mandatory to know the “metabolic” status at the time of development of BRVO.

BP Check, Hemogram (including peripheral blood morphology), Blood sugar, Lipid profile, Basic coagulation profile, ESR.

Selected patients: ANA, ANCA, RA factor, Chest X-ray, Montoux test, Protein C, Protein S, Antithrombin III, Lupus Anticoagulant, Homocysteine or any other investigation as per the clinical suspicion.

Ocular investigations

OCT

Timing: It can be performed any time starting immediately after the onset of symptoms. Asymptomatic patients with good vision may not require OCT as the chances of macular edema are less.

It is a useful tool for monitoring treatment response and also to diagnose recurrent edema.

Fundus fluorescien angiography (FFA)

First time: Better to be deferred till the time of near total disappearance of retinal hemorrhages which usually takes 1-3 months.

Repeat testing: Whenever there is suspicion of intraocular neovascularization.

Treatment

Observation

Early: Good vision, No macular edema, Limited area of involvement (macular BRVO)
Late: Compensated BRVO

Anti-VEGF (Avastin/Lucentis)

Intravitreal injection of anti-VEGF agents is the most widely practiced mode of therapy during early stages of BRVO these days.

The edema disappears within 48-72 hours in most cases. The disappearance of edema is so dramatic in most cases that non-response raises doubt about efficacy of the vial used! But the effect is short-lasting. Repeat injections are needed at 2-4 month intervals to maintain whatever benefit the patient gets after first injection.

There is no difference among the two agents in terms of efficacy.

Steroids

Topical, subtenon, intravitreal and oral routes of administration have been described. Among them, intravitreal and, to some extent, subtenon routes are supposed to be effective modalities. Intravitreal triamcinolone acetonide was the first agent which was found to be useful in resolving macular edema in cases of vein occlusion.

Cases of inflammatory vein occlusions and pseudophakic eyes benefit most from steroid therapy.

Intravitreal implants (Ozurdex) are supposed to give longest resolution period for macular edema.

Issues of cataract formation/progression and IOP elevation restrict the use of steroids as first line therapy in phakic eye
and steroid responders. Also, steroids have limited role in retinal ischemia and preventing neovascularization³.

NSAIDs
Nepafenac or bromfenac are useful adjuncts to steroids or anti VEGF agents to treat CME. They are not recommended as monotherapy.

Retinal Laser
BVOS has well established the role of green laser in treatment of BRVO. It has to be noted that the study was published in pre-OCT and anti-VEGF era!

Recommendations of BVOS

For Macular edema, Visual acuity of 6/12 or worse

- Wait for clearance of retinal hemorrhages to allow adequate fluorescence angiography
- Determine if decreased visual acuity is caused by macular edema (versus macular nonperfusion – on FFA)
- If macular edema explains vision loss, and no spontaneous improvement occurred by 3 months, grid macular laser photocoagulation is recommended
- If capillary non perfusion explains decreased visual acuity, laser treatment is not advised

For neovascularization

- Good quality of FFA has to be obtained after retinal hemorrhages have cleared sufficiently.
- If more than five disc diameters of capillary nonperfusion are present, the patient should be followed at 4 month intervals to see development of neovascularization.

- If neovascularization develops, panretinal photocoagulation to the involved sector should be applied using green laser to achieve medium white burns to cover entire involved segment

These guidelines are still valid in late stages of disease as the response to therapy is supposed to be permanent.

Vitrectomy
Indicated in complicated cases of Vitreous hemorrhage, TRD and CRD.

Treatment of risk factors
Strict metabolic control by timely referral to internist is of utmost importance not only for efficient ocular treatment but also to prevent further similar episodes in either eye and also in other systems of body.

Debatable issues

Investigating for rare systemic diseases
In cases of BRVO in young patients with uncertain etiology, these investigations are supposed to be advised to diagnose rare coagulation or connective tissue disorders. These include testing for protein C, protein S and antithrombin III among others. Most of the times, they are expensive and the results are equivocal and most of the internists don’t have a clue about what needs to be done if an investigation comes positive!

Observation vs treatment
Recent practice pattern by many clinicians includes use of anti-VEGF in all cases as soon as the patient presents. The point in favor of this practice is early inhibition of retinal ischemia. But, it is preferred that in cases with no CME, limited retinal involvement and good vision it is better to observe than treat.

Timing of treatment
In cases having less vision and significant CME, how early one should intervene is a matter of debate again. After the advent of anti-VEGF, the recommendation of BVOS to wait for 3 months is no more valid as accepted and practiced by almost all of clinicians these days. Only issue is how early to intervene?

Proponents of early intervention claim that early reversal to normal structure helps restoring normal function and inhibits after effects of ischemia. Others point out that, the cases which may get compensated later on with formation of collaterals also get treated without need if early therapy is given. This issue is clearly debatable as there is no clear evidence in support of either argument.
Anti VEGF vs Steroids vs Laser

As on today there is no direct comparative study to answer this question. The protocol practiced by many is as follows:

1) Obtain OCT to diagnose / document CME
2) Anti-VEGF or intravitreal steroids to start with
3) Repeat injections if CME recurs before disappearance of retinal hemorrhages
4) Obtain FFA after hemorrhages clear
5) Sectoral PRP laser or macular grid laser as described in BVOS. Observe, if there is no NV or CME.

Number of sittings of therapy

Regarding intravitreal anti-VEGF, there are proponents of PRN-based treatment as practiced in management of CNVM. There is no well established protocol regarding number of injections or treatment sittings required as many cases show recurrent edema even after repeated injection for more than 2 years. But, it is widely accepted that well done sectoral PRP laser need not be repeated and results in permanent cure in most cases.

Sectoral laser PRP for persistent or recurrent CME

BVOS has recommended macular grid laser only for persistent CME. Sectoral PRP laser is recommended only for cases of neovascularization. But, after the advent of anti-VEGF and steroids as treatment modalities, short lasting effect and the need for repeated injections has prompted many clinicians to consider sectoral PRP as a permanent cure even for cases of recurrent CME. As there are no randomized controlled trials with newer treatments, these debatable issues remain unanswered today.

References