INTRODUCTION

Since first approved by United States food and drug agency in 2004, Bevacizumab is an anti-VGEF or often known by the name of Avastin® has been frequently used in the medical world. Initially, the Anti-VGEF therapy is used for the treatment of metastatic colorectal cancer, used together with 5-fluorouracil-based chemotherapy. However, the high concentration of VEGF in any eye diseases that include the occurrence of neovascularization or / and inflammation such as proliferative diabetic retinopathy, neovascular glaucoma uveitis age-related macular degeneration (ARMD) and retinal vein occlusion provide new ways to treat disorders of the eye. By 2013 it is estimated up to 90% of retina specialists in the United States using anti-VGEF therapy for the initial treatment of loss of vision caused by eye disease with neovascularization. Intravenous injection of anti-VGEF reported superior to laser photocoagulation of the macula and became the standard treatment for diabetic macular edema.

Central Retinal Vein Occlusion first reported by Richard Liebrich in 1855. In Australia, Central Retinal Vein Occlusion (CRVO) were obtained at 0.1% -0.5% of middle and upper age groups, in India, 0.8% of adults. CRVO is classified into two spectrum of disease: mild (non-ischemic) and severe (ischemic). To mild spectrum CRVO (non-ischemic) found partial retinopathy, perfused or venous stasis whereas for severe spectrum (ischemic), found at least 10 disc areas of non - perfusion retinal capillary of the posterior polar with fluorescein angiography images are also referred to as nonperfused, complete or retinopathy hemorrhagic.

In CRVO management, the Association of American eye specialist (AAO) also recommends the use of Anti-VGEF in one handling CRVO. However, the use of Bevacizumab was also reported to have some undesirable effects such as: tolerance / tachyphylaxis, stroke, heart disease and organ failure such as kidney dependent on VEGF.

Purpose of this review is to summarize suggestions and best advice regarding pharmacotherapy of Bevacizumab as an anti-Vascular Endothelial Growth Factor (VGEF) that can be used as a therapy Central Retinal Vein Occlusion (CRVO).

Bevacizumab

Bevacizumab is a monoclonal antibody that inhibits the function of VEGF formation. Bevacizumab is produced from hamster ovaries in a nutrient medium containing the antibiotic gentamicin. Since it was first approved by the food and drug supervision agencies USA, Bevacizumab was first used to inhibit angiogenesis as a treatment for colorectal tumors in combination with chemotherapy 5-fluorouracil. A study with a total of 392 patients were randomly divided into three groups. Each group were then given monthly injections with anti-VGEF each 0.5 mg, 0.3 mg and observation alone for six months. After six months, the study subjects gave a mean average increase as many as 14.9 in the first group, 12, 7 in the second group and the third group of 0.8 letters - letters ETDRS. The same thing was reported by Epstein et al and dallen et al with Bevacizumab and CRVO. After research for 6 months (Epstein et al) and 12 months (dallen et al).

Now, Anti VEGF then become a standard treatment for Retinal Neovascularization and inflammation, including Bevacizumab.

CENTRAL RETINA VEIN OCCLUSION

Central Retinal Vein Occlusion first reported by Richard Liebrich in 1855. In Australia, Central Retinal Vein Occlusion (CRVO) were obtained at 0.1% -0.5% of middle and upper age groups, in India, 0.8% of adults. Some causes of CRVO are:

1. Vein emphasis of sclerotic retinal arterial,
2. Blood hy perviscosity such as polycythemia, hyperlipidemia and macroglobulinemia,
3. Retinal periphlebitis both central and peripheral retina.
4. The increase in intraocular pressure and
5. local causes such as orbital cellulitis.

CRVO is classified into two spectrum of disease: mild (non-ischemic) and severe (ischemic). In mild spectrum CRVO (non-ischemic) we found partial retinopathy, perfused or venous stasis whereas for severe spectrum (ischemic), found at least 10 disc areas of non - perfusion retinal capillary of the posterior polar with fluorescein angiography images are also referred to as nonperfused, complete or retinopathy hemorrhagic.

Therapy recommended by the American Association of Ophthalmology in the form of:

i) intravitreal corticosteroids
ii) intravitreal Anti - VEGF Treatment
iii) Surgery using LASER or other methods such as making anastomoses between retinal vein and choroidal circulation with a high-powered LASER application, radial optic neurotomy to suppress the central retinal vein and retinal vein canulation by administering tissue Plasminogen Activator (IPA).

VGEF dalam hubungannya dengan CRVO

The pathogenesis of CRVO is still not clearly understood.
Blockage of the central retinal vein hypothesized to occur in the posterior lamina cribrosa. Factors such as local anatomical abnormalities, changes in blood vessel walls, and hemorologic thrombotic tendency are predisposing factors. The central retinal artery share the same sheath with central retinal vein, this resulted in compression of the arteries which can lead to compression of the veins, especially in the arteries that are already sclerosis. This suppression may also result in thrombus formation. VEGF may result in increased permeability between the blood-retinal barrier and the blood-brain. At CRVO there is an increased intraluminal pressure and interstitial caused by blockage of blood vessels which results in a decrease in arterial perfusion which eventually became arteriinsufficiency and ischemia. Retinal ischemia is then stimulates the formation of Vascular Endothelial Growth Factor (VEGF) which resulted in the leaking of blood vessels and retinal macular edema to hemorrhage and capillary nonperfusion exacerbation.

Unwanted effects of Bevacizumab intravitreal injection

There are still much we do not know about bevacizumabtherapy, some of which is the right time to start treatment, when to terminate therapy, long-term efficacy and safety.

An international survey of Intravitreal Bevacizumab safety survey 2006 summarize that as much as 0.21% of Bevacizumab administration gives undesired effects. These effects such as corneal abrasion, trauma to the lens, endophthalmitis, retinal detachment, inflammation, or uveitis, progression of cataracts, loss of vision acute, Central Retinal Artery Occlusion (CRAO), subretinalbleeding, tear retinal pigment epithelium, increased blood pressure, transient ischemic attack, cerebrovascular damage and death.

Sharma S et al concluded that the subjects were given Bevacizumab has the potential 12 times greater risk of severe intracocular inflammation. Use of Anti-VEGF also has problems with tolerance / takipiliaks.

Several studies have found that injection of anti-VEGF can be absorbed throughout the body (systemic). This absorption can cause stroke in patients with a history of heart disease, damage to the VEGF-dependent organs such as kidney, microangiopathic hemolytic anemia and thrombocytopenia nonimmune with schistocytes.

This known side effect, gives doctors chances to make prevention of unwanted effects in the treatment of intravitreal injection of Bevacizumab for instance:

i) Intravitreal injections should be performed by an experienced ophthalmologist.

ii) Increase and decrease the dose interval therapy, discontinue therapy if there takipiliaks, combine drug with another method, replacing drugs (eg with other anti-VEGF).

iii) Checking serum creatinine, urine protein levels and blood pressure in the treatment package.

iv) Only do the therapy to improve the effectiveness and efficacy of therapies

v) To do strict follow up and early intervention in case of complications

CONCLUSION

Beside unwanted side effect, administration of bevacizumabintravitreal injection as Central Retinal Vein Occlusion therapy still the treatment of choice. Known unwanted side effect can be used to mitigate Bevacizumabintravitreal injection risk. Preinjection patient profile need to be conditioned to the risks that may occur.

With the understanding and consideration of the costs, advantages and disadvantages of Bevacizumabintravitreal injection therapy, considerate the best therapy for patients with Central Retinal Vein Occlusion (CRVO).

Reference


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