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Short Communication

Neovascular Age-related Macular Degeneration – Changing Paradigms in Management

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Introduction

Age-related macular degeneration (AMD) is a leading cause of central visual loss in patients over the age of 65 years. The exudative or neovascular form of AMD is characterized by Choroidal Neovascular Membrane (CNV) or serous Retinal Pigment Epithelial (RPE) detachments. It accounts for over 90% of the cases with severe visual loss. Complications such as subretinal hemorrhage, vitreous hemorrhage, fibrosis and scarring are responsible for poor visual outcome. The goal of therapy is to preserve vision and prevent further deterioration in patients with neovascular form of the disease. Treatments targeting Vascular Endothelial Growth Factor (VEGF) have been shown to improve vision in patients with neovascular AMD and now constitute the mainstay of therapy.

Medical management: The current recommendation based on the AREDS2 study is vitamin supplementation consisting of 500 mg vitamin C, 400 IU vitamin E, 10 mg lutein, 2 mg zeaxanthin, 80 mg zinc and 2 mg copper.

Treatment of Neovascular AMD

Photodynamic therapy

Verteporfin photodynamic therapy (PDT) is a laser treatment that selectively generates free radicals resulting in cytotoxic damage and occlusion of new vessels with regression of CNV after intravenous administration of a sensitizing agent. In the anti-VEGF era, the use of PDT has declined due to its relatively lower efficacy in improving visual acuity.

Anti- VEGF therapy

Anti-VEGF agents are currently the standard first-line therapy for the management of neovascular AMD. Bevacizumab has been successfully used as an off-label drug. Clinical trials suggest that monthly injections are required for sustained benefit. Frequent dosing may be associated with risks of progression of geographic atrophy. There may be a higher risk of stroke, endophthalmitis, retinal tears and detachments. The Lucentis Compared to Avastin Study (LUCAS) trial suggested Bevacizumab is an effective treatment option comparable to Ranibizumab [1].

Conbercept for neovascular AMD: Conbercept (KH 902) is a novel recombinant soluble VEGF receptor protein in which the binding domains of VEGF receptors 1 and 2 are combined with the Fc portion of Immunoglobulin G (phase III trial) [2].

Pharmacotherapeutic approach

- **Designated Ankyrin Repeat Proteins (DARPins):** Constitute a novel class of genetically engineered anti-angiogenic binding proteins that demonstrate high specificity and affinity (Phase III trial) [3].
- **Platelet Derived Growth Factor (PDGF) antibody:** Fovista is an aptamer-targeting PDGF - B homo-dimer that binds to its receptor PDGF-B found on pericytes for its recruitment, regulation and survival. In addition, PDGF-B has an important role in angiogenesis similar to VEGF [4].
- **Gene therapy:** Intraocular delivery of nuclear material using viral vectors in order to permanently alter tissue function at the cellular level.
- **rAAV.sFlt1:** Soluble fms-like tyrosine kinase-1 (sFlt1) is a soluble VEGF receptor that binds and reduces free circulating VEGF, thereby disabling vascular growth and proliferation [5].

Combination therapy

Currently, combination of Ranibizumab, Corticosteroidss and PDT may be used as second-line therapy for patients unresponsive to conventional monotherapy [6].

- Anti-VEGF and PDT
- Intravitreal Corticosteroids and PDT
- Combination of anti-VEGF agent, intravitreal corticosteroids and PDT

Advances in drug delivery to the posterior segment

- **Encapsulated cell technology:** NT-503
- **Refillable reservoir devices:** Mini-drug pumps provide preprogrammed drug doses into the vitreous cavity for 9 months [7].
- **Colloidal drug carriers:** Consist of liquid suspensions of microparticles/nanoparticles or liposomes [8].
- **Suprachoroidal drug delivery**

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