Commentary: Interfere with the Interface?

Ashwin Mohan, Ramesh Venkatesh

Department of Vitreoretina, Narayana Nethralaya, Bengaluru, Karnataka, India

Correspondence to: Dr. Ashwin Mohan, 121/c Chord Road, 1st Block, Rajajinagar, Bengaluru - 560 022, Karnataka, India.
E-mail: drashwinm@gmail.com

Anti-vascular endothelial growth factor (VEGF) agents have transformed the treatment of age related macular degeneration (ARMD); however, there still remain a significant proportion of nonresponders. Apart from lifestyle, genetic factors and tachyphylaxis, the role of the vitreo–macular interface (VMI), has been considered among the contributory factors.[1]

It was observed that fewer patients with wet or dry age related macular degeneration (AMD) have complete posterior vitreous detachment (PVD) as compared with controls.[2,3] There are four important principles one needs to keep in mind when understanding the role of VMI in the disease pathogenesis.[1] First, the presence of vitreo-macular traction (VMT) promotes a low-grade inflammation that potentiates the disease activity. In addition, VMT can also damage the retinal pigment epithelium (RPE) cells thus increasing the RPE VEGF. Second, when there is an absence of PVD, it is hypothesized that there is decreased oxygenation at the retinal surface, which can lead to higher VEGF levels. Third, the presence of PVD allows cytokines sequestered close to the retina to easily diffuse away, thus decreasing the concentration of VEGF for disease activity. Last, based on a similar logic, the injected anti-VEGF drugs are able to diffuse better when there is a presence of PVD, thus achieving higher therapeutic levels at the location of disease activity.

Few studies have shown that anti-VEGF treatment can be less effective in eyes with vitreo-macular adhesion (VMA) as compared to without VMA.[4-6] The potential therapies include vitrectomy and pharmacological vitreolysis.[1]

Vitrectomy has been shown to be helpful in eyes with poor response to anti-VEGF agents by improving visual acuity and reducing retinal thickness.[7] Taking into account the financial, logistic, and patient-safety factors involved, it is not appropriate to recommend vitrectomy for all cases of neovascular age related macular degeneration (nAMD); there are some patients, however, especially those with VMT, who appear to benefit from vitrectomy. More studies are needed to confirm this hypothesis.[1] Pharmacological vitreolysis involves alteration of the molecular organization of the vitreous in an effort to reduce or eliminate its role in disease. Microplasmin has been shown to be effective clinically for the induction of PVD in the MIVI-1 trial.[8] To prove its effectiveness in nAMD with focal VMA, the MIVI-5 trial – a randomized sham injection controlled double masked multicenter study – is currently underway. If microplasmin, or other vitreolytic agents, can be shown to efficiently and safely resolve VMA or relieve VMT, they may offer an exciting adjunct in the management of nAMD.

However, a study in the current issue of the Indian journal of Ophthalmology shows no significant difference due to the status of the VMI on the treatment outcomes of anti-VEGF injections.[9] Hence, further evidence is needed to clearly establish the role of VMI in nonresponders. Before using vitrectomy or pharmacological vitreolysis in the management of nAMD, we must, thus, proceed with caution carefully weighing the risks of the above treatments with their potential benefits.

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