Debate on the various anti-vascular endothelial growth factor drugs

Dear Editor,

We read with interest the article “A comparative debate on the various anti-vascular endothelial growth factor drugs: Pegaptanib sodium (Macugen), ranibizumab (Lucentis) and bevacizumab (Avastin)” by Nagpal et al.1

Herein, we demonstrate another potentially useful aspect of pegaptanib sodium in comparison with ranibizumab and bevacizumab, not mentioned in the above article.

Vascular endothelial growth factor-A (VEGF-A) has been recognized as an important neuroprotectant in the central nervous system.2,3 Receptors for VEGF-A are also present in normal retinal neuronal cells,4 indicating a possible functional role for VEGF-A in the neural retina. Recently, Nishijama et al. demonstrated that VEGF-A is a survival factor for retinal neurons and a critical neuroprotectant during the adaptive response to ischemic injury.6 Perhaps, the most surprising finding in their study concerned the reliance of normal retinal ganglion cells (RGCs) on VEGF-A for survival. Through both direct quantification of RGC numbers and assessment of optic nerve axon viability, they observed a dose-dependent decrease in neuron numbers after VEGF depletion with an antibody that blocks all VEGF isoforms. Interestingly, when the effects of VEGF were blocked with pegaptanib, which binds to VEGF164 and does not bind to VEGF120, there was no decrease in retinal RGC viability. VEGF164-treated eyes after ischemia showed obvious signs of disseminated intraretinal hemorrhages, suggesting an increase in vascular leakage caused by the VEGF164 treatment whereas no retinal hemorrhage was detected in the VEGF120-treated eyes.6 To conclude, the use of selective anti-VEGF agents such as pegaptanib, which inhibits pathologic VEGF164 and spares all other VEGF isomers, is strongly recommended to preserve retinal neurons in the long term, especially in the context of ischemic retinal diseases.

Mohammad Reza Khalili, MD; Hamid Hosseini, MD

Shiraz University of Medical Sciences, Department of Ophthalmology, Pooshtchi Eye Research Center, Iran.

Correspondence to Dr. Hamid Hosseini, Shiraz University of Medical Sciences, Department of Ophthalmology, Pooshtchi Eye Research Center, Iran.

E-mail: hosseinih@sums.ac.ir
The protective effect of ischemic preconditioning substantially decreased the number of apoptotic retinal cells. Ischemia-reperfusion injury increased VEGF-A levels and the expression of other pro-inflammatory cytokines. Ischemic preconditioning 24 h before photocoagulation was associated with increased VEGF-A in a model of ischemia-reperfusion injury.

We thank Khalili et al. for their valuable comments. Horozuglu et al. have highlighted the importance of selective anti-VEGF agents in the context of retinal ischemia-reperfusion injury. However, the authors have not mentioned the details of this finding. The authors have also raised the question of whether VEGF-A inhibition is more effective in ischemia-reperfusion injury compared to ischemia. The clinical application of VEGF-A inhibition is promising, especially in response to ischemia in animal models. The clinical application of VEGF-A inhibition is promising, especially in response to ischemia in animal models. The clinical application of VEGF-A inhibition is promising, especially in response to ischemia in animal models.

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