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,[4,5] 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.

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