Increased levels of vascular endothelial growth factor in aqueous humor of patients with diabetic retinopathy: Is it the whole truth?

Dear Editor,

The article “Increased levels of vascular endothelial growth factor in the aqueous humor of patients with diabetic retinopathy” by Selim et al. IJO, Vol 58: 2010, was interesting. They have demonstrated elevated levels of vascular endothelial growth factor (VEGF) in aqueous humor of the diabetic patients with proliferative retinopathy and also a strong correlation between aqueous VEGF levels and severity of the condition.1

However, it is equally crucial to understand the role of other etiological factor/s in the pathogenesis of the disease. One such important factor is Insulin like growth factor 1 (IGF 1). Unfortunately, I did not find the mention of IGF 1 anywhere in the article, though the Insulin like growth factor 1 has been seriously implicated in the pathogenesis of diabetic retinopathy.

The articles about the increased intra ocular fluid levels of VEGF in diabetic retinopathy, first appeared in the literature in 19942 and the authors here have simply reconfirmed it in 2010. The conclusion of this study thus, merely reaffirms the results of many earlier studies carried out around 20 years ago, and a casual reader may inaccurately attribute a significant role to VEGF in diabetic retinopathy, ignoring the other important factors. Since the present study does not show any different or new result, that could further the management of diabetic retinopathy, role of IGF 1 in the etiopathogenesis of diabetic retinopathy should have received attention, if not more, at least in the discussion section.

It’s pertinent to remember that IGF 1 is a key, direct regulator of VEGF levels and blood-retinal barrier breakdown in early stages of the disease3 and that, VEGF itself is a slave mediator activated by hypoxia and by the interaction between IGF 1 and IGF 1 surface receptor (IGFR 1).

The IGF 1 interaction with IGFR 1 in the retinal pigment epithelial and retinal vascular endothelial cells, initiates an intra cellular cascade, leading to a number of reactions. One of the by, products of that cascade reaction is increased production and potentiation of VEGF. The VEGF merely plays a secondary role to IGF 1 in the initiation and progression of diabetic retinopathy. The former is even unable to sustain its angiogenic activity in the absence of IGF1.4 Since the regression
of diabetic retinopathy following intra vitreal anti-VEGF injection, is neither universal nor uniform, there has/have to be other etiological factor/s of diabetic retinopathy, besides VEGF. The critical role played by the IGF 1 in the initiation and progression of the diabetic retinopathy is well recognized and has been lucidly detailed in the article by Smith et al.[4] The intraocular VEGF mirrors the elevated vitreous and retinal tissue levels of IGF 1. The elevation of IGF 1 precedes the onset of diabetic proliferative retinopathy, and a positive correlation has been observed between concentrations of IGF 1 in serum or vitreous fluid and extent of neovascularization in diabetic retinopathy.[5]

There are ongoing trials for modifying the IGF 1/IGFR 1 action to reverse or prevent the diabetic retinopathy.[6]

Strict metabolic control of the diabetes is essential to prevent the progression of retinopathy.

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