Neuronal cell death in the inner retina and the influence of vascular endothelial growth factor inhibition in a diabetic rat model
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Purpose: An increasing amount of evidence demonstrates that the function of neuronal cells in the diabetic retina is compromised before overt changes in vessel structure mediated by vascular endothelial growth factor (VEGF). The purpose of this study was to investigate changes in neuronal cells of the inner retina and to evaluate the effect of inhibiting VEGF in a streptozotocin (STZ)-induced diabetic rat model.

Method: VEGF inhibition was performed by intravitreal VEGF-A antibody injection at 1, 4, and 8 weeks after STZ injections.

Results: Following anti-VEGF treatment, apoptosis in retinal ganglion cells (RGC) increased and novel apoptosis in amacrine/bipolar cells of the inner nuclear layer (INL) was present by TUNEL staining. Phosphorylated-Akt (phospho-Akt) expression was significantly greater in RGCs but was decreased in the neuronal cells of INL after anti-VEGF treatment by western blot analysis and immunohistochemical staining.

Conclusion: These results demonstrate that RGC apoptosis is increased subsequent to VEGF inhibition in the diabetic retina. More importantly, VEGF inhibition significantly increased neuronal cell apoptosis in the inner nuclear layer of a diabetic retina, which seems to consist primarily of amacrine and bipolar cells. The phospho-Akt pathway, which plays a neuroprotective role via VEGF, was significantly affected by VEGF inhibition. This study shows that inhibiting VEGF may have detrimental effects on the apoptosis of neuronal cells in the inner layers of diabetic retina.