Diabetic Retinopathy — Diagnostic and Treatment Novelties

Blocking growth hormone or insulin-like growth factor 1 (IGF-1) are possible treatments for diabetic retinopathy (DR). Maria B. Grant, MD, University of Florida, Gainesville, FL, explained that GH and IGF-1 antagonists can produce significant reduction in neovascularization and reduction in the number of patients progressing to blindness. Diabetics with DR hypersecrete GH, while those with a GH deficiency have a lower risk of developing DR. The mitogenic effects of GH are mediated by IGF-1, explained Dr. Grant.

Octreotide, a somatostatin agonist (SSTR), also offers potential benefits in the fight against DR. Octreotide works by blocking growth hormone secretion, and a dose of 200-5000 µg/day for 15 months has been shown to reduce progression to high-risk proliferative DR (PDR). Octreotide may also retard DR progression and delay time to laser surgery (Grant et al. *Diab Care* 2000).

Study 802 and Study 804 are two randomized controlled Phase 3 trials with octreotide in DR. Both were designed to determine the efficacy of octreotide in delaying time to progression of DR. The subjects in Study 802 had more severe DR compared to those in 804, who were at baseline. Study 804 showed that octreotide 30 mg IM delayed time to progression of DR, with a statistically significant difference between active treatment and placebo (p=0.0430). The major secondary endpoints of macular edema and visual acuity did not show a statistically significant difference between active treatment and placebo in either study.

Is the eye a risk marker for CV morbidity and mortality?

According to Gabriella Tikellis, BSc, PhD, University of Melbourne, Melbourne, Australia, yes it is. She believes that there is a strong biological basis for performing retinal exams. "Retinal circulation is the window to systemic circulation," she explained. "Recognized and unrecognized risk factors impact directly on vascular structure and function. Retinal vessels share similar anatomy, physiology and pathology to brain and heart circulation, in people with hypertension. The retina offers a unique opportunity to non-invasively investigate the relationship of arteriolar/venular characteristics to the development of cardiovascular disease."

M.V. van Hecke, MD, PhD, VU Medical Center, Amsterdam, The Netherlands, however, maintains that the eye is not a risk marker for CV morbidity and mortality. "Today, there is limited and conflicting evidence about the relationship of retinal microvascular abnormalities with macrovascular disease," he said.

As evidence of his claim, Dr. van Hecke noted that the ARIC Trial (Klein, et al. *ATVB* 2000) found that general arterial narrowing is not associated with preventing cardiovascular disease or stroke, and that the severity of DR is not associated with stroke or coronary heart disease. He cited his own study, the Eurodiab Study (van Hecke, et al. *Diab Care* 2005), which determined that proliferative retinopathy led to a higher mortality risk than non-proliferative retinopathy, a finding that was upheld by the Valpolicella Heart Diabetes Study (Taugher, et al. *Diab Care* 2006).

"Retinal microvascular disease is not associated with large arterial endothelial dysfunction or subclinical atherosclerosis. No evidence is provided that retinal microvascular disease is a marker of microvascular dysfunction that causes large artery endothelial dysfunction and/or early atherosclerosis," he concluded.