Diabetes, Mild Cognitive Ills Found Linked

BY MARY ANN MOON
Contributing Writer

Patients with type 2 diabetes are at risk for amnestic mild cognitive impairment, which is thought to be a precursor of Alzheimer's disease, reported Dr. José A. Luchsinger and his associates at Columbia University, New York.

Diabetes is known to raise the risk of Alzheimer's disease (AD), but its relation to mild cognitive impairment (MCI) has not been established until now. Some researchers and physicians have described mild cognitive impairment, particularly amnestic MCI, as a transitional state between normal cognition and AD, the investigators wrote.

The calculated risk of MCI attributable to diabetes was 9% overall, 8% for African Americans, 11% for Hispanics, and 5% for whites.

Dr. Luchsinger and his associates studied the relationship between diabetes and MCI using data from a longitudinal cohort study of 918 Medicare recipients residing in New York City. Baseline data were collected from 1992 to 1994, and the subjects were followed every 18 months until 2003. They underwent extensive physical and neurologic examinations, including a battery of neuropsychological testing that assessed learning, memory, orientation, abstract reasoning, language, and visuospatial ability.

Seventy percent of the study population was women, and the mean age was 76 years. The study group was 44% Hispanic, 34% African American, and 22% white. Twenty-four percent of the subjects reported having diabetes.

Cognitive impairment was diagnosed by a consensus of two neurologists, one psychiatrist, and two neuropsychologists. A total of 334 cases of MCI developed during follow-up, including 160 cases of amnestic MCI.

Diabetes was significantly related to MCI of any cause, and even more strongly related to amnestic MCI, even after the data were adjusted to account for subject age, sex, ethnicity, years of education, stroke history, hypertension, heart disease, smoking, and apolipoprotein E gene status.

The calculated risk of MCI attributable to diabetes was 9% for the overall study population, 8% for African Americans, 11% for Hispanics, and 5% for whites, "reflecting the differences in diabetes prevalence by ethnic group," the investigators noted (Arch. Neurol. 2007;64:570-5).

"Diabetes could be related to a higher risk of AD and amnestic MCI through direct mechanisms, affecting the amyloid accumulation that is the putative culprit of AD, or indirect mechanisms, namely cerebrovascular disease," Dr. Luchsinger and his associates wrote.

However, their results suggested that the association is independent of cerebrovascular disease.

"Hyperinsulinemia …may disrupt brain amyloid β clearance by means of the insulin degrading enzyme. Another potential mechanism is the generation of advanced products of glycosylation," the researchers added. ■

Bevacizumab Found to Stabilize or Improve Macular Edema in Short-Term Study

BY JEFF EVANS
Senior Writer

Intravitreal injections of bevacizumab may stabilize or improve macular thickness and visual acuity after only 1 month in patients with diabetic macular edema, according to findings from a short-term, uncontrolled, retrospective study.

Dr. J. Fernando Arevalo of the Clinica Oftalmológica Centro Caracas (Venezuela) and colleagues reported the results of 6 months of follow-up after the treatment of 78 eyes in 64 diabetic macular edema patients with off-label bevacizumab (Avastin), which is a complete, full-length humanized antibody that binds to all subtypes of vascular endothelial growth factor (VEGF). VEGF is known to increase retinal vessel permeability, which occurs to an excessive degree in diabetic macular edema and results in the leakage of fluid and plasma constituents that thicken the retina as they pass into it.

'Intravitreal bevacizumab injections may have a beneficial effect on macular thickness and visual acuity, independent of the type of macular edema.'

Systemic therapy with bevacizumab is approved by the Food and Drug Administration for use in combination with other therapies for the treatment of metastatic colorectal carcinoma and recurrent or metastatic nonsquamous, non–small cell lung cancer.

The best-corrected visual acuity of the patients significantly improved from an average minimum angle of resolution of 7.4 minutes of arc to 4 minutes of arc 1 month after an injection of either 1.25 mg or 2.5 mg bevacizumab. The mean retinal thickness of the 1-mm central retina decreased from 387 mcm to 287.9 mcm after the first month, as measured by optical coherence tomography. Although these outcomes continued to improve slightly during the next 5 months of the study, neither outcome at the 6-month follow-up was significantly better than it had been at 1 month, according to the investigators.

There was no significant difference in either outcome between patients who had proliferative diabetic retinopathy and previous panretinal photocoagulation and those with nonproliferative diabetic retinopathy and macular edema (Ophthalmology 2007;114:743-50).

A majority of the 78 eyes improved by at least two lines of letters (based on the Early Treatment Diabetic Retinopathy Study) of best-corrected visual acuity (55%) or remained stable (41%) at the end of 6 months. Most of the eyes (81%) were initially treated with 2.5 mg bevacizumab, whereas others (19%) received 1.25 mg. About 20% of patients who received either initial dosage later needed one or two additional injections of the medication. Outcomes were similar between each dosage group.

No episodes of inflammation or severe losses of vision occurred immediately after injection, and no ocular or systemic adverse events were reported during the 6-month study.

"Our results indicate that intravitreal bevacizumab injections may have a beneficial effect on macular thickness and visual acuity, independent of the type of macular edema that is present (focal vs. diffuse). Therefore, in the future this new treatment modality could replace or complement focal/grid laser photocoagulation," or perhaps laser photocoagulation could "consolidate the results obtained with one intravitreal bevacizumab injection and decrease the need for reinjections," the researchers wrote.

Bevacizumab needs to be evaluated in a multicenter, randomized, controlled trial with longer follow-up before it is possible "to make any specific treatment recommendations," the investigators advised. ■

Elderly With Depressive Symptoms Have Higher Likelihood of Developing Type 2

BY MARY ANN MOON
Contributing Writer

Older adults who report a high degree of depressive symptoms are more likely to develop type 2 diabetes than are those without depressive symptoms, according to Mercedes R. Carnethon, Ph.D., of Northwestern University, Chicago, and her associates in the Cardiovascular Health Study.

Several studies have found an association between depressive symptoms or clinical depression and diabetes, but this is the first to examine the issue in a population of people over age 65, who have a high prevalence of both disorders, Dr. Carnethon and her associates said in the Archives of Internal Medicine.

The researchers assessed data on 4,681 participants in the Cardiovascular Health Study, which took place from 1989 to 1999. Depressive symptoms had been evaluated annually using the 10-item Center for Epidemiological Studies Depression Scale.

A minimum score of 0 for each item would indicate that the subject experienced that depressive symptom never or rarely, and a maximum score of 3 for each item would indicate that the subject experienced that symptom most of the time or always. Total scores of 8 or more points, out of a possible maximum of 30 points, were considered high.

Twenty percent of the participants had high depressive symptom scores on at least one occasion. The proportion of subjects who were overweight or obese—a factor that could potentially confound the association with diabetes—was similar across those who had low, intermediate, or high depressive symptom scores.

New-onset diabetes was determined by subjects' use of insulin or oral diabetes medications and by fasting glucose levels measured on two occasions during follow-up. A total of 234 subjects developed diabetes.

A high number of depressive symptoms on a single occasion, a significant increase in such symptoms over time, and persistently high symptoms over time all were associated with an excess incidence of diabetes, the investigators reported (Arch. Intern. Med. 2007;167:802-7).

The strongest link with diabetes was found when depressive symptom scores rose by at least 5 points over time.

"These findings were present across demographic strata and persisted with statistical adjustment for known correlates of depression and diabetes, such as BMI [body mass index], physical activity, cigarette smoking, alcohol intake, and C-reactive protein level," Dr. Carnethon and her associates said.

In summary, high depressive symptoms might be connected to the development of diabetes in older adults, and this association might not be attributable solely to adverse health behaviors or weight gain. "The pathophysiologic mechanism for this association remains unclear," they said.

Inflammation is often proposed as a likely mechanism, because inflammatory markers are associated with both diabetes and depression. However, the findings of this study showed no attenuation of the link between the two disorders when the data were adjusted for C-reactive protein levels. This suggests that "other biological mechanisms previously proposed, such as hypothalamic-pituitary-adrenal axis dysregulation and sympathetic nervous system stimulation, may be more salient," they added. ■