Women, Men Differ in Prediabetes Development

BY NANCY WALSH
New York Bureau

Women who progress from normoglycemia to prediabetes have greater endothelial dysfunction than do men who similarly progress, a study has found.

It has previously been shown that women with impaired glucose tolerance have a more atherogenic risk profile than men, and that this is evident years before clinical diabetes develops—an observation that led to the "ticking clock" hypothesis that attributes diabetic patients' risk for coronary heart disease to a long-standing atherogenic state.

New data from patients enrolled in the Western New York Study, an epidemiologic case-control investigation that originally looked at alcohol intake and cardiovascular disease risk, now have demonstrated that emerging risk factors such as markers of endothelial dysfunction, inflammation, and fibrinolysis/thrombosis also are elevated early in women who develop prediabetes.

The women who progressed from normoglycemia to prediabetes were older than matched controls and had higher levels of triglycerides and fasting glucose.

Among the study's 1,455 participants, 52 women and 39 men whose fasting serum glucose levels were below 100 mg/dL at baseline had levels between 100 and 125 mg/dL at a 6-year follow-up visit, according to Richard P. Donahue, Ph.D., of the department of social and preventive medicine, State University of New York at Buffalo, and colleagues (Diabetes Care 2007;30:354-9).

The women who progressed from normoglycemia to prediabetes were older than matched controls and had higher mean waist circumference, higher levels of triglycerides and fasting glucose, higher values on the homeostasis model assessment of insulin resistance (HOMA-IR), and a greater frequency of hypertension.

Aside from these conventional atherogenic risk factors, the women also had higher age-adjusted levels of biomarkers including human soluble intercellular adhesion molecule-1, E-selectin, and plasminogen activator inhibitor-1 (PAI-1).

In contrast, men who progressed from normoglycemia to prediabetes had higher levels of C-reactive protein and higher values on the HOMA-IR, compared with controls, without showing increased levels of the markers of endothelial dysfunction.

Dr. Donahue and his colleagues from Buffalo and from the University of North Carolina at Charlotte noted that previous studies have shown that elevations of E-selectin and PAI-1 are independent predictors of both type 2 diabetes and coronary heart disease. Elevated PAI-1, reflecting impaired fibrinolysis, is one of the most predictive of biomarkers, possibly working through a different pathway than do the cellular adhesion molecules, they said.

The markers of endothelial dysfunction that were elevated in women in this study and that predicted progression to prediabetes were independent of the effects of age or body mass index and HOMA-IR, according to the investigators. ■

Chronic Disease Care Uneven At Community Health Centers

BY KATE JOHNSON
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A national quality improvement initiative significantly improved several aspects of care for diabetes, asthma, and hypertension at community health centers, but had no impact on intermediate outcomes, according to a recent study.

"The substantial room for improvement in the postintervention period suggests the need for continued refinement of these methods," wrote Dr. Bruce E. Landon of Harvard Medical School, Boston, and colleagues (N. Engl. J. Med. 2007;356:921-34). "There is still much to learn about the tools and methods for quality improvement and their potential effectiveness."

The study compared the quality of care at 44 community health centers before and after their participation in the quality-improvement Health Disparities Collaboratives. This initiative, sponsored by the Health Resources and Services Administration, the Agency for Healthcare Research and Quality, and the Commonwealth Fund, was designed to improve care at community health centers, a particularly relevant target because of their "prominent role in providing care for members of minority groups and other disadvantaged populations," the authors noted. Since 1998, about two-thirds of community health centers (645) have participated in the collaboratives, but to date there has been no evaluation of their effect, they wrote.

The 44 intervention centers enrolled in the quality-improvement collaborative were matched with 20 control centers which had never participated in a quality-improvement collaborative. In addition, 40 of the 44 intervention centers also served as internal controls. Sequential, random samples of patients with diabetes, asthma, or hypertension were selected during the 1-year period before the intervention and the 1-year period after its completion. A total of 9,658 patients with one of the three conditions were selected: 3,392 with asthma; 2,904 with diabetes; and 3,362 with hypertension. Percentage scores for overall quality of care and composite scores for prevention and screening, disease monitoring and treatment, and outcomes were then calculated.

The study found that overall, when considering all three conditions, the intervention centers improved their care 4.9% above internal controls and 4.5% above external controls. In the composite score for prevention and screening, intervention centers also improved 6.2% more than internal controls and 4.5% more than external controls. And intervention centers also improved significantly more than controls in the composite score for disease monitoring and treatment (5.9% over external controls and 5.5% over internal ones).

When results were divided according to the three conditions, the overall trend was evident in centers focusing on asthma and diabetes, but not in those focusing on hypertension.

With regard to specific measures within the centers, the percentage of patients receiving antiinflammatory medication for persistent asthma, the percentage of patients with an asthma management plan, the percentage of diabetes patients with two or more assessments of glycated hemoglobin levels, and the percentage of patients advised about smoking all increased more in the intervention centers, compared with the control centers.

The authors offered several explanations for the lack of effect with respect to intermediate outcomes, including that many of the processes of care that were studied are linked to longer-term outcomes. In addition, "intermediate outcomes may require more intensive interventions in order to overcome environmental factors that pose particular challenges for patients treated at community health centers," they noted. ■

Safety Confirmed for Inhaled Insulin in Interim Analysis

BY NANCY WALSH
New York Bureau

NEW YORK — The safety of inhaled insulin is holding up at 2 years in an ongoing study, with adverse pulmonary effects being small, occurring early, and proving reversible on cessation of the drug, Dr. Jay S. Skyler said at a meeting sponsored by the American Diabetes Association.

An interim analysis of a 5½-year multinational study that includes 441 patients with type 1 diabetes has found that declines in pulmonary function—most likely age related—were similar among patients randomized to receive either subcutaneous or inhaled insulin (Exubera, Pfizer) plus basal insulin.

The mean changes in forced expiratory volume in 1 second at 3 months for inhaled and subcutaneous insulin were –0.047 and –0.026, respectively, and at 24 months the mean changes from baseline were –0.104 and –0.082. Only at the 3-month time point was the difference between the groups statistically significant, and concerns that changes in pulmonary function would progress—which would have been a real worry—have not been borne out, said Dr. Skyler, professor in the division of endocrinology, diabetes, and metabolism at the University of Miami, and the study's lead investigator.

There also have been concerns that repetitive inhalation of insulin particles could result in cumulative insults and the long-term development of fibrosis or tumors. "But the statistical likelihood of a few drops of powder or liquid hitting the same spot on a repetitive basis is trivial to nonexistent," he said, noting that the surface area of the adult human lung approximates that of a tennis court.

Among the 217 patients receiving inhaled insulin who completed the first 2 years of the trial, there was a 33% reduction in risk of severe hypoglycemia compared with those receiving the drug subcutaneously (Diabetes Care 2007; 30:579-85).

Patients receiving inhaled insulin did develop antibodies at an increased rate, said Dr. Skyler. Mean insulin antibody levels at baseline were 4.50 and 4.15 mcU/mL in the inhaled and subcutaneous groups, respectively. At 2 years, the respective levels were 64.5 and 3.85 mcU/mL. "When a substance is taken in through the lung, the immune system reacts in a Th2 fashion, favoring antibody formation," he said. However, the antibodies do not appear to interfere with efficacy or to be associated with adverse effects, he added.

Researchers also looked at efficacy in the interim analysis, and found that glycemic control was sustained and similar in both groups. Decreases in fasting glucose were greater in the inhaled insulin group, and weight gain was significantly less.

"If it works and doesn't appear to have any major problems, and is priced not very differently from other insulins, why has it done so poorly in the marketplace?" Dr. Skyler said.

Since Exubera was approved in January 2006, marketing efforts have focused specifically on endocrinologists. "I would submit that endocrinologists are the wrong target audience. We are not the ones who encounter the patients who are reluctant to use insulin," he said.

"By the time patients reach us, with our team of nurse practitioners and educators, we can get people onto injected insulin with ease," Dr. Skyler continued. Primary care physicians are more likely to see patients unwilling to go on injected insulin, and whether the use of inhaled insulin will increase when marketing efforts begin to target them remains to be seen, he said. ■