Diabetic Cardiomyopathy Drugs In Pipeline Will Boost Identification

BY JOYCE FRIEDEN
Associate Editor, Practice Trends

WASHINGTON — Diabetic cardiomyopathy is likely to become a more common problem in diabetic patients, but several new therapies in the pipeline look promising, Dr. Francisco Villarreal said at a meeting sponsored by the National Hispanic Medical Association.

“This is something we will have to watch for in our young people developing diabetes, and it takes a long time to evolve,” said Dr. Villarreal of the division of cardiology at the University of California, San Diego. The term “diabetic cardiomyopathy” will become much better known in the near future, Dr. Villarreal predicted. The term “refers to pathological changes in the hearts of certain diabetics in the absence of an identifiable cause,” he said. “Very frequently we associate diabetes with atherosclerosis, but in these patients we could not identify problems with blood vessels or the presence of hypertension. But we could document changes that occurred at the cellular level—be it muscle cells or cells that produce fibrous tissue—and also at the tissue level. These structural changes are characterized by myocardial hypertrophy and also by the presence of excess fibrotic tissue—in particular, collagen,” he explained.

Diabetic cardiomyopathy appears to play a role in the increased rate of heart failure in diabetic patients, according to Dr. Villarreal. The Strong Heart Study concluded that the extent and frequency of diastolic dysfunction was directly proportional to level of hemoglobin A1c (Circulation 2000;101:2271-6). The Framingham heart study led to similar conclusions (Prog. Cardiovasc. Dis. 1989;27:235-70).

When they looked at the risk of heart failure in diabetics and nondiabetics, in adult diabetic males, the risk was about two times that of [nondiabetic males], and in females, it was about five times,” he said. “But even worse, these risks multiplied about twice when observing young individuals—in young males, it was a four times higher risk, and in young females, eight times higher. It was also noted that each 1% elevation in HbA1c levels led to an increase of about 50% in the risk of heart failure.”

In one study, Doppler echocardiography documented the presence of diastolic dysfunction in up to 50% of well-controlled type 2 diabetic patients, Dr. Villarreal noted (Diabetes Care 2001;24:5-10). Two compounds in the therapeutic pipeline appear promising, he noted. Early studies of ruboxistaurin, a novel highly selective inhibitor of protein kinase C-β, suggest that it may curb diabetes-related blindness, nephropathy, and neuropathy. None of these trials involved cardiac diseases, but “it is likely that these drugs probably will also benefit the heart,” he said. The second compound, an anti-fibrotic (ALT-711), may help collagen become more compliant, Dr. Villarreal said.

Previous experience breast-feeding increased the likelihood of long-term exclusive breast-feeding in the diabetic mothers, and higher education levels (more than 10 years of school) increased the likelihood sevenfold, the investigators said.

“While there were trends toward less success in long-term breast-feeding among diabetic and nondiabetic mothers, compared of those who had a vaginal delivery, but these did not hold up as independent predictors after multiple logistic regression analysis. The small number of smokers in the study may have reduced the odds of finding an association between smoking and lactation, an association identified in previous studies. The investigators studied all women with type 1 diabetes delivering consecutively at the hospital from May 2001 to February 2003. The results did not include two women who did not want to participate because of an investigator’s vacation, and one woman who could not be identified 4 months after delivery.

In the first retrospective study, the diabetic women were offered prenatal classes with information on breast-feeding and a visit to the neonatal intensive care unit. In addition, a diabetes nurse specialist offered individual counseling on the benefits of breast feeding and described the possibility of using a breast pump if the infant’s ability to suck was impaired.

Neonates stayed with their mothers for the first 2 hours of life, and 47% first breast-fed during the first feeding. Then they were admitted to the neonatal intensive care unit for 24 hours, where they received artifactual feedings of mother’s milk or low-protein formula milk, mainly by nasogastric tube. Every 3 hours to prevent hypoglycemia. During that time, they also averaged two breast-feedings. Severe hypoglycemia in 30% of infants was treated with IV glucose.

The rate of breast-feeding during this early period might have been improved if the mothers had been allowed to sleep near the infants. In a neonatal ICU, the investigators suggested.

“We believe that the [prenatal] classes and individual counseling about benefits and difficulties of breast-feeding offered to the women were valuable,” Ms. Stage, and her associates wrote.

Age, Gender May Flag Risk for Serious Infections in Diabetics

BY PATRICE WENDLING
Chicago Bureau

Nice, France — Male gender, advanced age, and a history of several office visits in the past year were among the risk factors for a complicated urinary tract infection in a retrospective cohort study of older primary care patients with type 2 diabetes mellitus.

The findings were used to create a clinical prediction rule that could improve management of UTIs in patients aged 45 years and older, Leonie Muller said at the 16th European Congress of Clinical Microbiology and Infectious Diseases. Patients with type 2 diabetes are known to be at greater risk for urinary tract infections. But little is known about predictors of a complicated course.

Although the rule still needs to be validated in other populations, the idea is to use it to identify patients at high risk for serious UTI and educate them about the signs and risk factors for complicated infection, she said.

In a second retrospective cohort study, Ms. Muller and colleagues at the University Medical Center Utrecht, the Netherlands, created a similar rule for predicting complicated lower respiratory tract infections, which are also common in older patients with diabetes.

Using data from the Second Dutch National Survey of General Practice, the investigators conducted a 12-month, prospective cohort study that identified 6,345 patients, 45 years or older, with type 2 diabetes. The primary outcome was the occurrence of a complicated course UTI, defined as an episode of acute pyelonephritis or prostatitis, and recurrent cystitis. The mean age was 67 years, 46% were male, and 55% were smokers. Multivariate logistic regression analysis was used to develop a clinical prediction rule.

There were 179 (2.8%) complicated UTIs, 1 per 100 patient-years in females and 2 per 100 patient-years in males. Independent predictors were increasing age (odds ratio 1.7), male gender (OR 1.8), 12 or more office visits in the previous year (OR 11.5), urinary incontinence (OR 2.4), cerebrovascular disease or dementia (OR 2.1-4), and renal disease (OR 5.6).

An example of how the rule might be applied in a diagnostic setting would be that a 75-year-old (1 point) male (1 point) patient with diabetes and renal disease (3 points) would be considered high risk, whereas his 73-year-old (1 point) wife with diabetes and urinary incontinence (2 points) would not. Ms. Muller, a doctoral student at the university, acknowledged that the model has the potential to identify a large percentage of high-risk patients, adding that future studies should focus on the cost-effectiveness of the rule.

In the second study, the investigators evaluated 20 predictors of death and/or hospitalization following an episode of lower respiratory tract infection in a subgroup of 1,694 patients, aged 65 years and older, with diabetes, from the same database. Among 445 episodes of lower respiratory tract infections including acute bronchiectasis, exacerbation of chronic obstructive pulmonary disease, asthma, or pneumonia, 13 were fatal and 55 required hospitalization.

Positive predictors of death and/or hospitalization were pneumonia (adjusted odds ratio 5.3), age greater than 80 years (OR 2.2), presence of heart failure (OR 2.1), and prednisone use (OR 2.4). The hospitalization/death rate was 5.2% among patients found to be at low risk and 35.6% among high-risk patients, Ms. Muller reported.

Type 1 Diabetes Needn’t Preclude Breast-Feeding

BY SHERRY BOSCHERT
San Francisco Bureau

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