ARBs Improve Endothelial Function, Findings Show

For patients with impaired glucose intolerance, angiotensin II receptor-1 blockade helps significantly.

BY PAM HARRISON
Contributing Writer

TORONTO — Endothelial function improves significantly with angiotensin II receptor-1 blockade in patients with impaired glucose tolerance, and quickly reverts to baseline after discontinuation of therapy, Thomas H. Schindler, M.D., reported at the annual meeting of the Society of Nuclear Medicine.

He and his colleagues at the University of California, Los Angeles, also saw a parallel and significant decrease in insulin resistance during 24 weeks of treatment.

The findings suggest that improved insulin sensitivity and the pleiotropic effects of renin-angiotensin-aldosterone system blockade may account for the reduction in new-onset type 2 diabetes that has been associated with the use of ACE inhibitors and angiotensin receptor blockers (ARBs).

The researchers set out to determine whether the insulin-sensitizing effects of ARB therapy with valsartan would improve endothelial-dependent vasomotion in 30 patients with IGT, defined as fasting glucose below 126 mg/dL and a 2-hour oral glucose tolerance test between 140 and 200 mg/dL.

"None of them had any other traditional coronary risk factors," Dr. Schindler said. Another 20 healthy volunteers were also studied at baseline and compared with the IGT patients; they received no medication during the study.

BMI was significantly higher in IGT patients than in controls. Both total cholesterol and low-density lipoprotein cholesterol were within the normal range.

The patients with IGT received valsartan, 160 mg a day for 12 weeks, after which the dose was doubled to 320 mg a day and continued for another 12 weeks. Treatment was discontinued at 24 weeks, and the patients were followed to 32 weeks.

"Body mass index was significantly higher in IGT patients than in controls, but both total cholesterol and low-density lipoprotein cholesterol were within the normal range and did not differ significantly between the two groups," Dr. Schindler said.

Not unexpectedly, myocardial blood flow responses from rest to cold pressor testing were significantly lower at baseline in the IGT patients than in the controls. In contrast, endothelial-independent stimulation of myocardial blood flow did not differ between the two groups.

After 12 weeks of valsartan at 160 mg a day, myocardial blood flow response to cold pressor testing significantly improved in the IGT patients, from 0.75 mL/g per minute at baseline to 0.89 mL/g per minute at 12 weeks.

After 12 more weeks of valsartan at 320 mg, myocardial blood flow response to cold pressor testing again improved significantly, from 0.89 mL/g per minute at 12 weeks to 0.94 mL/g per minute at 24 weeks. Valsartan was discontinued for 8 weeks; the observed reaction to cold pressor testing disappeared.

In parallel fashion, insulin sensitivity—expressed as the glucose infusion rate during hyperinsulinemia euglycemic clamp—increased steadily in the IGT patients, from a baseline value of 3.2 mg/kg per minute (a clear sign that patients were insulin resistant) to 3.7 mg/kg per minute at 12 weeks and to 4.2 mg/kg per minute at 24 weeks.

At 32 weeks, the improvement in insulin sensitivity in the IGT patients had returned to baseline. In a later interview, Dr. Schindler speculated that the pleiotropic effects of the ARB—including potential anti-inflammatory, antioxidative, and antithrombotic properties—may have all helped to improve insulin sensitivity.

"We conclude that IGT in patients without other coronary risk factors is associated with coronary endothelial dysfunction and that angiotensin II receptor-1 blockade with valsartan restores endothelial function. This effect was independent of the plasma lipid profile and C-reactive protein, an inflammatory plasma marker, suggesting that these beneficial effects on the coronary endothelium may be related to an increase in insulin sensitivity and the pleiotropic effects of ARB blockade," Dr. Schindler said. ■

Better Glucose Control in Those Who Know A_{1c} Goal

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Nearly half of adult patients who received care at a municipal hospital diabetes clinic did not recognize the term A_{1c}, and fewer than one-quarter knew what their hemoglobin A_{1c} level should be, Mary K. Rhee, M.D., reported at the annual scientific sessions of the American Diabetes Association.

"This lack of recognition and knowledge occurs despite a formal diabetes education and reinforcement at each patient visit," said Dr. Rhee of the department of medicine at Emory University, Atlanta.

"However, patients who recognize the term A_{1c} and know the goal have better glycemic control. In light of these findings, education programs should include strategies that ensure that patients achieve and retain appropriate understanding of A_{1c} and the A_{1c} goal," she said.

To test a theory that patients who know the American Diabetes Association goal for hemoglobin A_{1c} level have better glycemic control, Dr. Rhee and her associates surveyed 97 patients who received care at a diabetes clinic affiliated with Emory University. All patients new to the clinic attend an 8-hour education program which includes instruction about the importance of glycemic control, what A_{1c} is, and what the A_{1c} goal is.

"The program begins at the initial visit and continues over several visits in the first 6 months," Dr. Rhee explained. "The nurse providers are also expected to routinely discuss individual A_{1c} results and reemphasize the A_{1c} goal with each patient."

The average age of study participants was 59 years, and 54% were female. Almost all the patients (95%) were African American, and their average body mass index was 35 kg/m^2. Four percent were being treated with diet alone, 30% were taking oral agents, and 66% were being treated with insulin.

The average duration of diabetes was 10 years, and time since the initial education was 6.5 years. Participants had an average of 3.7 visits to the clinic per year, and the mean A_{1c} level of study participants at the time of the survey was 7.8%.

Based on their response to the question, "What should your A_{1c} be?" patients were divided into three groups. Group 1 consisted of those who did not know either the A_{1c} term or the A_{1c} goal (47%), group 2 recognized the A_{1c} term but did not know the goal (30%), and group 3 knew both the A_{1c} term and the correct A_{1c} goal (23%).

Even though patient characteristics were similar in the three groups, those in group 3 had lower A_{1c} levels (6.9%), compared with their counterparts in group 2 (7.7%) and group 1 (8.4%).

Moreover, knowing the A_{1c} term and goal was independently associated with lower A_{1c} levels after the investigators adjusted for other risk factors. Poor patient knowledge was independently associated with higher A_{1c} levels.

Fewer than 45% of patients in groups 1 and 2 were able to reach an A_{1c} level of less than 7%, while 64% of those in group 3 reached that goal.

"Therefore, better patient knowledge was associated with better glycemic control," Dr. Rhee concluded. ■

Glycemic Control Unchanged Despite Changes in Tx Strategies

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Despite a rise in the number of treatment regimens for adults with type 2 diabetes during the 1990s, national surveys showed no improvement in the number of adults who achieved glycemic control, Tao Fan reported in a poster session at the annual scientific sessions of the American Diabetes Association.

'This trend does not improve the rates of cardiovascular, renal, and other diabetic complications that may have an impact on health care costs.'

The finding suggests "there should be more aggressive therapy—particularly pharmacotherapy—for type 2 diabetes patients," Mr. Fan told FAMILY PRACTICE NEWS.

He and his associates analyzed a sample of 1,215 subjects from National Health and Nutrition Examination Survey III (NHANES III, 1988-1994) and 758 subjects from NHANES 1999-2002.

All subjects reported a diagnosis of type 2 diabetes and had data on diabetes medication and hemoglobin A_{1c} levels, Mr. Fan said. He is a doctoral student in the department of pharmaceutical health services research at the University of Maryland, Baltimore.

The researchers defined four therapeutic regimens: diet only, insulin only, oral antidiabetic drugs (OADs) only, or OADs plus insulin.

From NHANES III to NHANES 1999-2002, glycemic control rates dropped from 44.3% to 39.8% in subjects aged 65 years and older, but increased from 15.8% to 16.2% in those aged 20-44 and from 39.9% to 44.0% in those aged 45-64.

Diet as sole therapy decreased from 27.4% to 18.7% between the two surveys, as did insulin-only therapy (from 24.2% to 14.0%).

At the same time, the use of OADs alone increased from 45.4% to 57.4% and the use of OADs plus insulin increased from 3.1% to 10%.

Mr. Tao and his associates adjusted the analysis for age, gender, ethnicity, body mass index, and duration of diabetes. When they adjusted for these factors, they found that the likelihood of insulin use only and diet only as diabetes treatment declined from NHANES III to NHANES 1999-2002, while the likelihood of OAD use only and OAD plus insulin use increased.

Multivariate analysis revealed no change in the likelihood of glycemic control between NHANES III and NHANES 1999-2002.

"This trend does not improve the rates of cardiovascular, renal, and other diabetic complications that may have an impact on health care costs," the researchers reported in their poster that was presented.

GlaxoSmithKline funded the study. ■