Microalbuminuria Risk Drops With Carvedilol

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O R L A N D O, F L a. — Treatment with carvedilol cut the incidence of new-onset microalbuminuria by 47%, compared with metoprolol, in a study of more than 700 patients with type 2 diabetes and hypertension.

Carvedilol’s ability to prevent microalbuminuria is probably due to its antioxidant properties—an effect that gives carvedilol an advantage over other -blockers and perhaps over other classes of antihypertensive medications as well, George L. Bakris, M.D., said at the annual meeting of the American College of Cardiology.

The findings should be taken into account when selecting an antihypertensive medication, especially for patients with type 2 diabetes, said Dr. Bakris, director of the Hypertension/Clinical Research Center at Rush University in Chicago.

Even one hypertension patient who does not have diabetes, carvedilol may be a good option if they have indications of impaired glucose control or if they have inflammatory markers, Dr. Bakris told this newspaper. However, he cautioned that this doesn’t mean that a patient whose diabetes is currently well controlled and who is tolerant of another -blocker or another antihypertensive regimen should be switched to carvedilol.

The new findings came from a pre-specified subanalysis of the study focused on the 88% of patients who had albuminuria at enrollment. The vast majority of these patients had a modest level, with a urinary albumin-to-creatinine ratio of less than 30 mg/dL. Of a total of 1,911 patients who had microalbuminuria, defined as a ratio of more than 30 mg/g but less than 301 mg/g; Microalbuminuria was the focus of this study because it reflects diffuse endothelial dysfunction in the renal vasculature and has been an independent predictor of cardiovascular events in patients with diabetes as well as in patients without diabetes. Microalbuminuria is also a marker of systemic inflammation that mirrors levels of high-sensitivity C-reactive protein.

Patients in the study were randomized to treatment with either carvedilol or metoprolol, and their dosages were titrated up-titrated over a 7-week period. Carvedilol treatment began at a daily dosage of 6.25 mg b.i.d and was increased as tolerated to a daily maximum of 25 mg b.i.d. metoprolol was started at 25 mg and was raised to a maximum dosage of 200 mg b.i.d. Patients who entered the study with a blood pressure of at least 140/90 mm Hg were treated to a pressure of 135/85 mm Hg or less. Those who began at a pressure of 130-139/80-89 mm Hg were treated to reach a goal pressure of 130/80 mm Hg or less.

After 5 months of treatment, 388 patients treated with carvedilol had an average drop in their urinary albumin to creatinine ratio of 14%, compared with an average increase in the ratio of 2.5% among 542 patients treated with metoprolol—a statistically significant difference.

Among the patients who began the trial with a ratio of less than 30 mg/g, 6.6% of patients treated with carvedilol developed new-onset microalbuminuria during the 5-month follow-up, compared with 11.1% of the patients treated with metoprolol—a statistically significant difference. Treatment with carvedilol cut the risk of developing microalbuminuria by 47%, compared with patients treated with metoprolol. Carvedilol was also more effective than metoprolol for cutting urinary albumin levels in patients who were normoalbuminuric when they started treatment.

The protective effect of carvedilol, compared with metoprolol, was independent of the drugs’ antihypertensive effects. The achieved blood pressures among patients in both groups were essentially identical. The led Dr. Bakris to speculate that carvedilol’s ability to prevent microalbuminuria was due to the drug’s antioxidant properties. He cautioned that reductions in microalbuminuria have not yet been proved to cut the rate of cardiovascular events.

FDA Issues Public Advisory on Crestor Dose in Asian Patients

Evidence of a heightened risk of rhabdomyolysis in Asian Americans led the Food and Drug Administration to issue an alert and to require a label revision for the statin rosuvastatin last month.

According to the FDA Public Health Advisory, in a phase IV pharmacokinetic study involving a diverse population of Asians residing in the United States, rosuvastatin (Crestor) drug levels were found to be elevated approximately twofold, compared with a Caucasian control group.

Because the risks of statin side effects have been shown to be dose dependent, change to the Dose and Administration section of the label was made to state that the 5-mg dose should be considered the starting dose for Asian patients, and any increase in dose should take into consideration the increased drug exposure in this patient population. The new label also emphasizes that 40 mg should not be used as a starting dose and should only be used in patients “who have not achieved their cholesterol goals with the 20-mg dose.”

All statins are known to create a risk of myopathy/rhabdomyolysis. In June, the FDA issued a public health advisory alert to physicians emphasizing that physicians should pay close attention to the rosuvastatin label regarding dosage, “to cut the risk of myopathy.”

Just days after the current advisory was released, Public Citizen renewed its call for the drug’s withdrawal, citing its own analysis of adverse event reports in which the rate of rhabdomyolysis per million prescriptions filled for rosuvastatin was 6.2 times higher than the rate for all of the other statins combined. The FDA denied the request, stating, “We do not believe that the adverse event reports on Crestor indicate the drug poses an unacceptable risk of rhabdomyolysis and that extensive preapproval and ongoing clinical monitoring indicates that rosuvastatin’s muscle safety is comparable to that of other statins.”

—Mark S. Lesney