High-Dose Atorvastatin Cuts HF Hospitalization

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DALLAS — Intensive treatment with atorvastatin in patients with stable coronary heart disease led to a significant reduction in hospitalization for heart failure in a secondary analysis of results from a study with 10,000 patients.

The results are the best evidence so far that statin treatment confers a heart-failure benefit. The findings also suggest that the benefit is not mediated by a reduction in ischemic coronary events but by another, as-yet unknown, mechanism, Dr. David D. Waters said at the annual scientific sessions of the American Heart Association.

"Randomized, controlled trials of statins in patients with heart failure will likely yield important findings," reported Dr. Waters, who is chief of the division of cardiology at San Francisco General Hospital.

The heart failure analysis was a prespecified, secondary analysis of the Treating to New Targets (TNT) study, which randomized 10,001 patients with stable coronary disease to daily treatment with 10 mg or 80 mg atorvastatin (Lipitor) and then followed them for a median of 4.9 years.

The primary end point of the study was the combined rate of coronary death, nonfatal myocardial infarction, resuscitated cardiac arrest, and stroke. The 80-mg daily dose of atorvastatin was significantly more effective than the 10-mg daily dose for preventing this end point (N. Engl. J. Med. 2005;352:1425-35).

The study was sponsored by Pfizer, which markets Lipitor. Dr. Waters has been a consultant to and a speaker for Pfizer, and he has also received research grants from the company.

The impact of treatment on heart failure was assessed by the number of hospitalizations for heart failure during the study.

A total of 164 patients (3.3%) on the 10-mg dose were hospitalized for heart failure, compared with 122 patients (2.4%) in the 80-mg group, a 26% relative risk reduction that was statistically significant, Dr. Waters said.

The study excluded those patients with New York Heart Association class IIIb and class IV heart failure, as well as patients who had a left ventricular ejection fraction at baseline of less than 30%. Among those who enrolled, 8% of the patients had heart failure at baseline, but this subgroup accounted for 38% of the hospital admissions for heart failure. Among those who entered the trial without heart failure, the incidence of heart-failure hospitalizations was 1.9%.

In patients with preexisting heart failure, the hospitalization rate was 17.3% in the 10-mg atorvastatin group, compared with 10.6% in the 80-mg group.

In the subgroup with preexisting heart failure, the impact of high-dose atorvastatin was even greater. The hospitalization rate was 17.3% among those who were on 10 mg, compared with 10.6% among those on 80 mg, a "very large" absolute reduction of 6.7%, and a relative risk reduction of 41% that was statistically significant, Dr. Waters said.

In a multivariate analysis, the reduction of low-density lipoprotein (LDL) cholesterol was a significant modifier of risk after adjustment for other clinical and demographic variables. For every 1% drop in the serum level of LDL cholesterol, the risk of hospitalization for heart failure fell by 0.6%.

There was no indication that the drop in heart failure hospitalizations was mediated by an effect of high-dose atorvastatin on the incidence of myocardial infarctions and other ischemic events. During the 3 months prior to their first hospitalization for heart failure, only 15% of the patients had an acute coronary event. That meant that 85% of the hospitalizations for heart failure were not triggered by a coronary event, Dr. Waters noted.

Several other beneficial effects of statins might explain an effect on heart failure, including improved endothelial function, inhibited production of inflammatory cytokines, and direct antifibrotic, antihypertrophic, or antioxidant effects. ■