Gout Linked to Worse Heart Failure Outcomes

BY MITCHEL L. ZOLER

ORLANDO — Gout boosted the risk of death or hospitalization for heart failure in an observational, case-control study of more than 150,000 patients with heart failure.

The analysis also showed that patients with heart failure and gout who were on long-term allopurinol treatment had a significantly reduced risk for death or heart failure hospitalization, Dr. George Thanassoulis said at the annual scientific sessions of the American Heart Association.

These findings do not warrant the use of allopurinol in heart failure patients without gout, but the data suggest that if such patients are candidates for allopurinol because of coexisting gout, then the new re-

sults "increase the reasons to treat them," said Dr. Thanassoulis, a cardiologist at Boston University and the Framingham (Mass.) Heart Study.

He hypothesized that allopurinol benefits heart failure outcomes not by lowering blood levels of uric acid, but by inhibiting oxidative stress and the endothelial dysfunction that oxidative stress produces.

The study used administrative health record data from res-

idents of the province of Quebec who were aged older than 65 years. Cases were 14,327 people hospitalized for heart failure but without another heart failure hospitalization during the 3 years before the index episode, a restriction that helped ensure a uniform level of heart failure severity among the patients. Controls were 143,255 people in the Quebec database matched to the cases by follow-up duration and by calendar year.

The average age was 79 years among the cases and 77 years among the controls. Both the cases and controls were evenly split among men and women. Identification of gout relied on hospitalization, a physician visit, or a diagnostic code in the medical record.

During an average follow-up of 2 years, the rate of death or new heart failure hospitalization was 63% higher in the patients with gout than in those without gout, a statistically significant difference in an analysis that controlled for several demographic and clinical variables including age, gender, comorbidities, and medications.

The risk for death or heart failure hospitalization was even higher in patients who had acute gout, with a twofold

higher risk in the adjusted analysis. The researchers defined acute gout as hospitalization or a physician visit for gout within 60 days of the index heart failure event.

Another pair of analyses looked at the impact of allopurinol treatment. Among patients with an index heart failure event who also had gout treatment with allopurinol, there was a significant 31% reduction in the subsequent rate of death or heart failure hospitalization in the adjusted analysis. This benefit was limited to the patients on chronic allopurinol treatment for more than 30 days. Patients on allopurinol for 30 days or less showed no significant reduction in mortality or new heart failure hospitalizations. ■

VITALS

Major Finding: The rate of death or new heart failure hospitalization was 63% higher in the patients with gout than in those without gout.

Data Source: The analysis used administrative health record data from residents of the province of Quebec; 14,327 cases of people hospitalized for heart failure were compared with 143,255 controls.

Disclosures: None

Iron Repletion Aids Heart Failure in Phase III Investigation

BY MITCHEL L. ZOLER

ORLANDO — The clinical benefits from intravenous iron in chronic heart failure seen in a placebo-controlled study of 459 patients abruptly made iron repletion a new, plausible treatment for a sizeable fraction of heart failure patients.

"This is a new therapeutic concept. When patients [with heart failure] are symptomatic, physicians should think about iron deficiency," Dr. Stefan D. Anker said at the annual scientific sessions of the American Heart Association. The study results also showed that the boost from iron occurred regardless of whether patients were anemic before starting treatment, a finding that suggests iron helps patients by a mechanism that does not involve hemoglobin.

The study findings "are very intriguing. Iron deficiency hasn't been on our radar screen," commented Dr. Mariell L. Jessup, professor of medicine and associate chief of clinical affairs in the division of cardiovascular medicine at the University of Pennsylvania in Philadelphia. "I think this is something that people will start to act on quickly."

"Iron deficiency is extremely common in this population," commented Dr. John G.F. Cleland, professor and chairman of cardiology at the University of Hull, England.

Despite the promising new results, Dr. Anker stressed that the study was not powered to adequately address safety or efficacy end points such as survival and hospitalization. Further study is needed to build up a larger experience with the tested agent, ferric carboxy-

maltose, in heart failure patients, although Dr. Anker's study included 150 patient-years of treatment with this drug with no hint of excess adverse events aside from an expected, modest increase in gastrointestinal disorders. Dr. Anker also expressed eagerness to test this strategy in patients with diastolic dysfunction: heart failure with preserved left ventricular function.

About 20%-30% of heart failure patients likely have iron deficiency, said Dr. Anker, professor in the Center for Cardiovascular Research at Charité University in Berlin. Dr. Cleland said this estimate probably underestimates the actual prevalence.

Iron deficiency is probably prevalent in many heart failure patients because of a combination of poor diet and poor gastrointestinal absorption, and because of increased bleeding linked with aspirin use, Dr. Cleland said.

The Ferinject Assessment in Patients With Iron Deficiency and Chronic Heart Failure (FAIR-HF) trial enrolled patients during June 2007–December 2008 at 75 sites in 11 countries. Dr. Anker and his as-

sociates screened more than 950 patients to find the 459 who fulfilled the study's criteria for heart failure and serum ferritin level. Eligible patients had either New York Heart Association class III heart failure and a left ventricular ejection fraction of 45% or less, or class II heart failure and an ejection fraction of 40% or less. Their hemoglobin at enrollment could be 95-135 g/L, and so the study included nearly equal numbers of patients with anemia (hemoglobin of 120 g/L or less) and those without (more than 120 g/L). Their average age was 68, and 82% had class III heart failure.

Patients were randomized on a two-to-one basis to receive an intravenous, bolus injection of ferric carboxymaltose equivalent to 200 mg iron weekly or placebo. Once iron repletion occurred, after 8 or 12 weeks, the dosage was scaled back to one injection every 4 weeks.

After 24 weeks, the self-reported Patient

Global Assessment was at least moderately improved in 50% of the 304 patients receiving iron and in 28% of the 155 patients on placebo, a statistically significant difference for this primary end point. New York Heart Association heart failure class improved in 47% of the patients on iron and in 30% of the control patients, also a significant difference in the second primary end point. The results appeared in an article published online (N. Engl. J. Med. 2009 Nov. 17 [doi:10.1056/NEJMoa0908355]) concurrently with Dr. Anker's report at the meeting.

During the study, mortality rates were 3% in the iron group and 6% in the control patients, a nonsignificant difference. Hospitalization for any cardiovascular reason occurred in 10% of the iron patients and 20% of the controls, a difference that came close to, but did not reach, statistical significance. Cardiac disorders of any type were significantly more common in the control patients, 50%, than in those on iron, 28%. The most notable adverse event more common in the iron patients was gastrointestinal disorder, in 17% of the iron patients and 7% of the controls, a difference that just missed statistical significance. ■

VITALS

Major Finding: At 24 weeks, Patient Global Assessment scores improved in 50% of the 304 heart failure patients receiving intravenous iron and in 28% of the 155 patients on placebo.

Data Source: FAIR-HF, placebo-controlled phase III study of 459 patients, from 75 sites in 11 countries, randomized to iron or placebo.

Disclosures: The study was sponsored by Vifor Pharma, a Swiss company that markets Ferinject in Europe. Dr. Anker has received fees from Vifor; he also has received fees from Roche and Amgen.

Despite its promising results, the study was not powered to address safety or efficacy end points.

DR. ANKER

'The Effect Occurs So Quickly'

MY TAKE

This is a remarkable result. I am especially impressed that the separation in the primary end points between the patients receiving iron and those on placebo began to be statistically significant after the first 4 weeks on treatment and then continued to separate further.

The effect occurs so quickly. This

is probably the fastest separation we've seen in a clinical trial in heart failure.

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