Erythropoietin May Improve HF-Related Anemia

BY BRUCE JANCIN

BARCELONA — Erythropoietin therapy in patients with anemia of heart failure resulted in improved exercise capacity, reduced heart failure symptoms, and decreased hospitalizations, and showed strong trends for reduced rates of MI and all-cause mortality in a meta-analysis of 11 small randomized clinical trials.

Moreover, erythropoietin was not associated with an increased rate of adverse events, as in some clinical trials carried out in the settings of cancer or chronic kidney disease. It may be that erythropoietin's angiogenesis-promoting effect is therapeutic in the context of heart failure but is the source of side effects in patients with cancer or renal disease, Dr. Dipak Kotecha said at the annual congress of the European Society of Cardiology.

He was quick to offer a caveat, however: "This is all based on a relatively small sample size. Some of these trials were small proof-of-concept trials, others were mechanistic and looked at the effects of different doses. None were individually powered for clinical events. The follow-up was relatively short, at 2-12 months."

The 11 randomized trials involved 794 patients with mild to moderate anemia and left ventricular systolic heart failure. Nine of the trials were placebo controlled. Mean baseline hemoglobin was 10.1-11.8 g/dL and rose by 2.0 g/dL in response to erythropoietin therapy.

This 2.0-g/dL increase in hemoglobin was associated with a mean 69-meter improvement in 6-minute walk distance compared with controls, a 96-second increase in exercise duration, and an improvement in New York Heart Association functional class equivalent to three-quarters of a class.

"All of these changes were clinically as well as statistically highly significant," observed Dr. Kotecha of Royal Brompton Hospital, London.

Peak oxygen consumption, or VO_2 max, increased by an average of 2.3 mL/kg per min. Left ventricular ejection fraction increased in erythropoietin-treated patients by an absolute 5.8% compared with controls; that is comparable to the improvement seen in the major clinical trials of beta-blockers. Quality of life scores using the standard Minnesota and Kansas City instruments showed significant gains as well.

Heart failure hospitalizations in erythropoietin-treated patients were significantly reduced by 36% compared with controls, reflecting an absolute 8% rate difference. "The absolute 8% decrease in hospitalizations for heart failure is very similar to what's been seen in the major clinical trials of beta-blocker therapy in heart failure," Dr. Kotecha said.

Heart failure hospitalizations in erythropoietin-treated patients were significantly reduced by 36%.

DR. KOTECHA

B-type natriuretic peptide levels fell by an average of 40%, or 237 pg/dL, in response to erythropoietin. Again, that is a magnitude of effect similar to what has been seen in clinical trials of combined beta-blocker and ACE inhibitor or angiotensin receptor blocker therapy, he continued.

The risk of all-cause mortality was reduced by 39% in the erythropoietin treatment group, a strong trend that just missed statistical significance. The 27% relative risk reduction in acute MI also was not quite significant. Definitive answers as to whether erythropoietin therapy has a beneficial effect on these key outcomes are anticipated from the ongoing Amgen-sponsored phase III Reduction of Events With Darbepoetin Alfa in Heart Failure (RED-HF) trial, which is randomizing more than 3,000 patients.

Anemia occurs in one-third to one-half of patients with heart failure and has been associated with a markedly worse prognosis. Dr. Kotecha cited as an example a Dutch meta-analysis involving more than 153,000 heart failure patients, 37% of whom were anemic. The mortality after a minimum of 6 months of follow-up was 30% in nonanemic patients and 47% among those with anemia (J. Am. Coll. Cardiol. 2008;52:818-27).

Dr. Kotecha reported having no financial conflicts of interest in connection with the meta-analysis, which was conducted using Cochrane Collaboration methodology and has been submitted to the Cochrane Review for possible publication. ■

Process-of-Care Intervention Improves Outpatient HF Care

BY DIANA MAHONEY

BOSTON — Performance improvement intervention for outpatient care of heart failure patients increases the use of evidence-based, guideline-recommended processes and therapies, Dr. Clyde W. Yancy said at the annual meeting of the Heart Failure Society of America.

Provision of prompts, pocket cards, check lists, and guideline-based decision-support algorithms significantly increases the likelihood that physicians will use evidence-based therapies, devices, and patient education, according to primary findings from the large-scale, prospective IMPROVE-HF (Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting) study.

After 24 months, significantly more patients received treatments for which they were eligible.

DR. YANCY

To assess conformity with established heart failure (HF) performance measures based on class I recommendations of the national HF guidelines (Circulation 2005;112:e154-235), the IMPROVE-HF investigators reviewed the charts of 35,000 HF outpatients treated at the study's 167 sites at baseline, then 12 and 24 months after the implementation of the practice-specific process-of-care initiative, said Dr. Yancy of Baylor University Medical Center at Dallas.

The baseline findings suggested suboptimal conformity with performance measures for all of the practices considered, and significant variation in the use of evidence-based, guideline-recommended therapies, especially for women and the elderly. Large variations were observed in the use of anticoagulation for atrial fibrillation, implantable cardioverter defibrillators (ICDs), cardiac resynchronization therapy (CRT), and HF education. In all, only 27% of patients who were assessed with HF at baseline were receiving treatments for which they were eligible, based on the guidelines, Dr. Yancy reported.

But 24 months after the start of the initiative, significantly more patients received treatments for which they were eligible, across nearly all measures, Dr. Yancy said. The largest changes were observed in the use of ICDs, aldosterone receptor antagonists, and CRT, from 39%, 35%, and 50% of eligible patients, respectively, to 68%, 60%, and 56%. Use of ACE inhibitors or angiotensin receptor blockers and beta-blockers, and the provision of HF education, also improved significantly.

Dr. Yancy reported having no financial disclosures relative to his presentation. The IMPROVE-HF study is supported by Medtronic Inc. ■

Trials Need to Include More Hispanics to Unravel Paradox

BY PATRICE WENDLING

CHICAGO — Despite the underrepresentation of Hispanics in heart failure trials, evidence has emerged suggesting that they have unique risk factors and outcomes that must be taken into clinical consideration.

The evidence also underscores the need to recognize the vast heterogeneity of Hispanics, Dr. Ileana Piña said at a meeting sponsored by the International Society on Hypertension in Blacks.

"Hispanics represent a cultural group, not a racially identifiable group," said the Cuban-born cardiologist. "You can't lump them all together."

But that's exactly what has happened. It wasn't until the 2000 U.S. census that the term "Hispanic" was changed to "Spanish, Hispanic, or Latino" to describe persons of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race.

Several studies have made the observation—coined the "Hispanic paradox"—that Hispanics have lower all-cause and cardiovascular mortality, despite increased obesity and diabetes, and lower socioeconomic status, said Dr. Piña, professor of medicine at Case Western Reserve University, Cleveland.

A study of Medicare enrollees found that Hispanics were 1.2 times more likely to be hospitalized for heart failure than were whites, while blacks were 1.5 times more likely. But after adjustment for sex and age, in-hospital mortality was significantly lower in Hispanics and blacks than in whites. A California study also showed that blacks and "Latinos" initially hospitalized with heart failure in 1991 or 1992 were more likely to be rehospitalized than were Asians and whites, but were less likely to die during the following year.

Sociocultural factors are often used to explain the Hispanic paradox, but more recent data are causing some to rethink the paradox or at least to differentiate Hispanics by birthplace. Among diabetics in the San Antonio Heart Study, age- and sex-adjusted hazard ratios indicated that U.S.-born Mexican-Americans have a 66% greater risk of all-cause and CV mortality, compared with non-Hispanic whites, while Mexico-born Mexican-Americans appeared to be at similar risk.

Greater representation in patient registries, research studies, and clinical trials is needed Dr. Piña said. Only one major heart failure trial, HF-ACTION, has specifically differentiated Hispanics, and those patients made up just 3%.

Greater elucidation of heart failure risk factors and outcomes in Hispanic populations could lead to more targeted therapies and risk modification. With one in three U.S. residents expected to be Hispanic by 2050, there is great urgency to act, said Dr. Piña, who disclosed serving as a speaker for AstraZeneca, Novartis, and Merck. ■

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