Drug does not improve outcomes for patients with advanced heart failure

August 2 2016

Among patients recently hospitalized with heart failure and reduced left ventricular ejection fraction (LVEF; a measure of heart function), the use of the drug liraglutide did not lead to greater post-hospitalization clinical stability, according to a study appearing in the August 2 issue of *JAMA*.

Heart failure is the leading cause of hospitalization in the United States with more than 4 million admissions per year from 2003-2009. Abnormal cardiac metabolism contributes to the pathophysiology of advanced heart failure with reduced LVEF. A class of drugs, glucagon-like peptide 1 (GLP-1) agonists have shown cardioprotective effects in early clinical studies of patients with advanced heart failure.

Kenneth B. Margulies, M.D., of the University of Pennsylvania, Philadelphia, and colleagues randomly assigned patients with established heart failure and reduced LVEF who were recently hospitalized to the GLP-1 agonist liraglutide (n = 154) or placebo (n = 146) via a daily subcutaneous injection; study drug was advanced to a dosage of 1.8 mg/d during the first 30 days as tolerated and continued for 180 days. The primary outcome for the study was a score in which all patients, regardless of treatment assignment, were ranked across 3 hierarchical tiers: time to death, time to rehospitalization for heart failure, and time-averaged proportional change in N-terminal pro-B-type natriuretic peptide level from study entry to 180 days. Higher values indicate better health (stability).

Among the 300 patients who were randomized, 271 completed the study. Compared with placebo, liraglutide had no significant effect on the primary end point. There were no significant between-group differences in the number of deaths (12 percent in the liraglutide group vs 11 percent in the placebo group) or rehospitalizations for heart failure (41 percent vs 34 percent) or for the exploratory secondary end points (primary end point components, cardiac structure and function, 6-minute walk distance, quality of life, and combined events). Prespecified subgroup analyses in patients with diabetes did not reveal any significant between-group differences.

"The GLP-1 agonist liraglutide did not improve posthospitalization clinical stability in patients with advanced heart failure and reduced LVEF despite prior studies indicating that GLP-1 therapy might ameliorate mechanisms of myocardial insulin resistance reported in patients with severe cardiomyopathies," the authors write.

"These findings do not support the use of liraglutide in this clinical situation."

More information: *JAMA*, doi:10.1001/jama.2016.10260