New study shows spironolactone reduces heart failure hospitalizations, but not mortality

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A late-breaking clinical trial, known as the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) trial, to be presented at the American Heart Association (AHA) Scientific Sessions, November 18, 2013, demonstrates that spironolactone did not reduce the primary outcome of cardiovascular death, heart failure hospitalization, nor surviving a cardiac arrest in patients with heart failure and preserved ejection fraction (pump function). However, spironolactone did reduce the major burden faced by these patients—the risk of repeated hospitalizations for heart failure.

The TOPCAT trial is the first randomized, double-blind trial to assess the effect of spironolactone on clinical outcomes in these patients with heart failure and preserved ejection fraction.

The trial enrolled 3,445 participants from 270 medical centers in six countries. Participants were randomly assigned to receive either spironolactone (target dose of 30 milligrams/day) or matching placebo, and were followed for an average of nearly 3.5 years. Moreover, participants were also treated for other co-existing conditions (e.g., diabetes, high blood pressure, etc.).

According to the researchers, patients randomized to spironolactone were less likely to be hospitalized for heart failure compared to those on placebo. At the end of the study, 206 out of 1722 patients on spironolactone (12 percent) had been hospitalized for heart failure, compared to 245 of 1723 patients (14 percent) given placebo. There were no statistically significant differences between the groups in deaths or hospitalizations from any cause.

The TOPCAT trial also presented the opportunity to study cardiac structure and function in this population through an echocardiography sub-study in 935 patients, which demonstrated a high prevalence of abnormal cardiac structure in these patients. These results will be published simultaneously with the TOPCAT AHA presentation in the AHA journal, *Circulation: Heart Failure*.

The TOPCAT trial was led by a clinical research team at Brigham and Women's Hospital (BWH) under the direction of Marc A. Pfeffer, MD, PhD, BWH Division of Cardiovascular Medicine, Department of Medicine, in collaboration with the New England Research Institutes, directed by Sonja McKinlay, PhD. The rationale for using spironolactone—an inexpensive, generic, medication—stems from the pioneering research of Bertram Pitt, MD, University of Michigan School of Medicine, who showed the benefit of this class of drugs in patients with heart failure and reduced ejection fraction, and who also served as chair of the TOPCAT Steering Committee.

"At present, therapy for this large proportion of patients with heart failure is empiric, and there remains a huge unmet need," said Scott Solomon, MD, director of BWH Noninvasive Cardiology, who also led the core echocardiography lab for the study.

"While these patients also suffer heart attacks and strokes, hospitalizations for heart failure represent their predominant problem, which is also a major burden to society," said Eldrin Lewis, MD, advanced heart failure specialist, BWH Division of Cardiovascular Medicine, Department of Medicine, who chaired the TOPCAT Clinical Endpoints Committee.

"When treating our patients, clinicians are always balancing risks and benefits," said Akshay S. Desai, MD, MPH, advanced heart failure specialist,

BWH Division of Cardiovascular Medicine, Department of Medicine. "The results of TOPCAT will help inform clinicians as they make treatment decisions for this understudied population," Added Desai, "If clinicians choose to use this therapy, they must be vigilant about monitoring for serum markers of kidney and electrolyte disorders which can be exacerbated by spironolactone."

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