New data from studies bolsters case for using aldosterone antagonists in heart failure

September 19 2011

Roughly 5 million people in the United States live with heart failure, a condition in which the heart is unable to pump blood around the body effectively. The causes and types of heart failure vary greatly, and treatment must be tailored to each patient. In some cases, doctors will prescribe a class of diuretic drugs called aldosterone antagonists. However, these diuretics may cause dangerously high levels of potassium in the blood (hyperkalemia) of certain patients, putting them at risk for sudden cardiac death. Therefore, it is crucial that doctors weigh the risks and benefits of prescribing aldosterone antagonists for their patients who have heart failure.

To help prescribers make the best decisions concerning these drugs, Bertram Pitt, MD, Professor of Internal Medicine at the University of Michigan School of Medicine, will review the data from three prominent studies during his presentation at the 7th International Symposium on Aldosterone and the ENaC/Degenerin Family of Ion Channels, being held September 18-22 in Pacific Grove, Calif. The presentation is entitled, "Potential Future Role of Mineralocorticoid Receptor Blockade in Patients with Heart Failure." The meeting is sponsored by the American Physiological Society.

Dr. Pitt will also outline a study in progress that will shed light on potential future uses of aldosterone antagonists, as well as discuss a compound currently in Phase II clinical trials that is designed to prevent or treat hyperkalemia.

EPHESUS and EMPHASIS-HF Results

Two studies for which Dr. Pitt was an investigator have shown that aldosterone antagonists reduce mortality in people with different symptoms. In 2003, the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival (EPHESUS) study demonstrated that treatment with eplerenone lowered the risk of cardiovascular mortality and cardiovascular complications 13% in people with systolic left ventricular (lower chamber) dysfunction and heart failure after a heart attack.

In 2010, the Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure (EMPHASIS-HF) study revealed the drug's benefit in a broader population, i.e., patients with chronic systolic heart failure and mild symptoms. There was a 24% reduction in cardiovascular death and a 42% reduction in hospitalization for heart failure in patients who took the drug compared to those who did not.

"These results where overwhelming," Dr. Pitt said, noting that the benefits were so clear that the trials were stopped early in countries where the drug was already on the market.

The study continued for another 10 months in countries where eplerenone was not available, thus providing additional data that Dr. Pitt said reinforces the earlier findings. Furthermore, a new sub-analysis of the study showed reductions in death and hospitalization in five different groups of high-risk patients with chronic heart failure and mild symptoms, including patients older than age 75 and patients who have diabetes. Although there was an increase in the incidence of hyperkalemia among patients in the high-risk groups who took eplerenone, there was no increase in serious hyperkalemia or hyperkalemia that warranted hospitalization. Dr. Pitt will discuss the most recent data and the new sub-analysis at the meeting.

RALES Study

An older study, the Randomized Aldactone Evaluation Study (RALES) published in 1999, showed a benefit in people with severe heart failure and reduced left ventricular ejection fraction who took the aldosterone antagonist spironolactone. (Ejection fraction is the fraction of blood pumped out of a ventricle with each heartbeat.) "Together, these three studies—EPHESUS, EMPHASIS-HF and RALES—provide the basis for why we think aldosterone antagonists are so important," Dr. Pitt said.

TOPCAT Trials

Finally, Dr. Pitt will discuss the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) study, a multi-center, international trial of spironolactone that began in 2006 and is still recruiting treatment centers and enrolling participants. Patients in this study have heart failure but have not experienced disturbed function in the heart's ventricles.

Hyperkalemia Remains a Concern

Although there is substantial evidence of the benefits of aldosterone antagonists, hyperkalemia remains a concern. To that end, researchers are currently investigating a compound called RLY5016 that is designed to prevent or treat hyperkalemia by binding to potassium and pulling it out of the blood. However, the compound is only in Phase II clinical trials and will not be ready for review by the Food and Drug Administration for several years.

Dr. Pitt is cautiously hopeful. "Many of the people who are at risk for cardiovascular death, such as those with a history of diabetes or high blood pressure, are not treated with these drugs because of the risk of

hyperkalemia," he said. "Ideally this compound would allow us to continue to use aldosterone antagonists in these patient groups, and in people with compromised renal and uretal function, who are at increased risk of hyperkalemia. But it is very early in the investigation and not proven by any means."

Provided by American Physiological Society