No benefit found from BP drug in treatment of recently hospitalized heart failure patients

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Despite high hopes that a blood pressure-lowering medication called aliskiren would help people following hospitalization for heart failure, no beneficial effects were found, according to research presented today at the American College of Cardiology's 62nd Annual Scientific Session.

Heart failure is the leading cause of hospitalization for people over age 65, costing Medicare billions of dollars annually, and researchers are always on the lookout for more effective treatments.

The Aliskiren Trial on Acute Heart Failure Outcomes (ASTRONAUT) is an international, double-blind study that enrolled stable patients hospitalized for heart failure and followed them after discharge. Patients were randomized to receive either aliskiren, starting at 150 mg and increasing to 300 mg, or placebo, in addition to other standard heart failure therapies. After six months, patients in both groups had a similar likelihood of cardiovascular death or re-hospitalization for heart failure.

However, patients in the aliskiren group did show a statistically significant and sustained drop in one of the study's secondary endpoints, blood levels of N-terminal proB-type natriuretic peptide (NT-proBNP)—a hormone that increases as heart failure progresses.

"In the majority of cases, patients' natriuretic peptide levels correlate with their stage of heart failure and can help physicians plan treatment," said Mihai Gheorghiade, MD, professor at Northwestern University's Feinberg School of Medicine and lead author of the ASTRONAUT

study. "It was surprising to see that our study drug did positively affect patients' levels of this peptide, but this positive effect did not translate into reduced mortality or hospitalizations as we would have expected."

While patients taking aliskiren in addition to evidence-based heart failure therapy showed improvements in natriuretic peptide levels over time, they also had significantly higher rates of hyperkalemia (overly high potassium levels), worsening renal function and hypotension (abnormally low blood pressure). According to Dr. Gheorghiade, it may be that the side effects of the treatment regimen "blunted" its beneficial effects.

"Just like if you give a patient with a blood clot that is causing a heart attack a medication that is effective in dissolving the clot but then that medicine causes bleeding—you may have stopped the heart attack, but this prevents the drug from being highly beneficial," he said.

ASTRONAUT enrolled 1,615 patients at 316 centers who were hospitalized for heart failure and were stable enough at discharge to safely receive high doses of aliskiren. Both groups were similar at baseline with stable kidney function, a low ejection fraction (reduced blood pumped by the heart) and high NTproBNP. Both groups also had similar rates of high blood pressure, coronary artery disease, diabetes and atrial fibrillation. Standard heart failure therapy was comparable between groups. Patients were initially followed every two weeks, and then every three months, for one year.

"Despite all the evidence-based therapies available for heart failure patients today, their chances of dying or returning to hospital are still unacceptably high," said Dr. Gheorghiade. "There is a huge unmet need to improve patient outcomes after discharge, which is what we were hoping our study would do."

Dr. Gheorghiade said that this particular patient population has a much higher mortality rate than outpatients with chronic heart failure, even though the problems that cause them to be hospitalized generally respond well to standard in-hospital therapies. Previous studies have shown that 30 percent of patients hospitalized for heart failure are readmitted within one to two months. This is significant because hospitalization is one of the strongest predictors of death among outpatient heart failure patients.

Among patients receiving aliskiren, the likelihood of death was reduced in patients without diabetes but not in those with diabetes. This may be due to the fact that people with diabetes are already at risk for conditions such as hyperkalemia, kidney impairment and hypotension that may be observed with aliskiren, particularly when used on top of other standard therapies. However, the exact mechanisms that cause opposite effects in patients with or without diabetes are not clearly understood and deserve further analysis, Dr. Gheorghiade said. He added that although these subgroup findings are intriguing, they must be interpreted with caution because of the statistical limitations of this type of analysis.

Similar adverse effects among patients with diabetes and renal impairment, along with an increased incidence of non-fatal stroke, led to the termination of another trial with aliskiren called ALTITUDE in 2011. The patients in the ASTRONAUT study were a completely different population, explained Dr. Gheorghiade. He further noted that the ASTRONAUT study did not reproduce the pattern of clinical outcomes observed in ALTITUDE, and in particular, aliskiren-treated patients in ASTRONAUT had a lower risk of stroke than the placebo group.

Dr. Gheorghiade recommended that additional studies be done among non-diabetic patients with heart failure to see whether renin inhibition can still deliver positive results.

More information: This study will be simultaneously published in the *Journal of the American Medical Association*, and will appear in the March 20 print edition with online release at the time of presentation.

Dr. Gheorghiade will present the study "The ASTRONAUT Study: Aliskiren Trial on Acute Heart Failure Outcomes" on Monday, March 11 at 11:15 a.m., in Moscone Center, South, Esplanade Ballroom.

Provided by American College of Cardiology