Heart failure drug less effective in real world

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A large study addressing the effectiveness and safety of aldosterone antagonist therapy for older heart failure patients has found notable differences between the drug's results in clinical trial vs. what occurs in actual practice, according to researchers at Duke Medicine.

Those differences have been noted anecdotally by doctors, and likely contributed to the slow adoption of aldosterone antagonists in clinical practice, but they had not been confirmed in a large study examining the drugs in real-world situations.

The Duke-led research, published Nov. 28, 2012, in the Journal of the American Medical Association, suggests that doctors should more closely model the types of patients and the procedures followed in clinical trials when prescribing drugs in practice.

"Understanding whether real-world effectiveness matches the efficacy of clinical trials is important to assure that we are implementing and providing the best care possible," said lead author Adrian F. Hernandez, M.D., MHS, a cardiologist and member of the Duke Clinical Research Institute. "We are in an era where drugs can be efficacious, and the question is can they be effective and safe in clinical practice as they're being used. That's where we find differences and need more comparative effectiveness studies."

Key efficacy trials decades ago reported impressive benefits of aldosterone antagonist therapy, but doctors have long had questions about its safety for older and sicker patients who may be at risk for

retaining high levels of potassium in their blood – a potentially fatal condition known as hyperkalemia.

Hernandez and colleagues used Medicare data to identify older patients who had been hospitalized for heart failure or weak pumping action called reduced ejection fraction. Among more than 5,880 eligible patients, 1,070 were discharged with prescriptions for aldosterone antagonist drugs, which inhibit sodium reabsorption in the kidneys to lower fluid retention and, as a result, improve heart function.

The research team found fewer benefits associated with the drugs than had originally been reported. There was no difference in deaths or hospital readmissions for cardiovascular events between the patients who went on the aldosterone antagonists and patients who did not. Patients taking the drugs were, however, less likely to be readmitted to the hospital for heart failure. At the same time, they were at significantly higher risk of readmission for hyperkalemia.

The study suggests that aldosterone antagonists might have limited success in reducing deaths among older patients. Potential reasons include a lack of adherence to therapy, and improper dosing and monitoring in practical use.

"Patient populations, monitoring, and procedures in clinical trials are different than in normal practice," Hernandez said. "High-risk patients, women and members of minority groups are typically underrepresented in clinical trials, while clinical trial participants tend to adhere to therapy and follow-up tests."

Hernandez said the study's findings highlight the importance of conducting clinical trials that can be easily generalized to real-world practice. At the same time, better protocols for aldosterone antagonist therapy could be established for doctors to ensure appropriate patient

selection, correct dosing, medication adherence and early follow-up visits to screen for hyperkalemia.

"We can't have a paradigm where we give a pill and say come back in three months," Hernandez said. "Developing systems that encourage optimal use and monitoring of aldosterone antagonist therapy may help ensure that the effectiveness of this therapy in clinical practice approaches what was achieved in clinical trials."

Provided by Duke University Medical Center