Irbesartan reduces heart failure in patients with quivering heart

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Most research in atrial fibrillation (AF) has focused on reducing stroke and other embolic events. Yet heart failure occurs more frequently in AF patients, but has not been the focus of intervention research.

In a major international trial, researchers from McMaster University in Canada, found that the hypertension drug irbesartan reduced the risk of heart failure complications and the combination of stroke, other embolic events and transient ischemic events, also known as ministrokes, in patients with atrial fibrillation.

Atrial fibrillation is a common disorder of the heart rhythm that causes the muscles of the atria to quiver instead of beat at regular intervals. The condition affects about one per cent of the population and up to 10 per cent of people over the age of 80. Although strokes are frequent in AF patients (and have been the focus of much research), heart failure is even more common, but no intervention has been shown to reduce this complication.

The findings of the ACTIVE-I (Atrial Fibrillation Clopidogrel Trial With Irbesartan for Prevention of Vascular Events) study will be presented today at the European Society of Cardiology in Barcelona, Spain, by Dr. Salim Yusuf.

Dr. Yusuf is a professor of medicine in the Michael G. DeGroote School of Medicine at McMaster University and director of the Population Health Research Institute at McMaster University and Hamilton Health

Sciences.

"The approach to the management of AF patients should be multidimensional," said Yusuf, the chair of the ACTIVE-I steering committee. "While antithrombotic drugs are important in preventing stroke and other complications, complimentary approaches to reducing these and other complications by lowering blood pressure or controlling heart rhythm are important."

The ACTIVE-I study is part of a larger program of research into atrial fibrillation and involves randomizing over 9,000 patients (enrolled at more than 500 centres in 41 countries) to receive irbesartan or placebo for 4.1 years. The study was completed in June, 2009.

The difference in systolic blood pressure between the groups was approximately 3 mm Hg. The study examined two co-primary outcomes: the composite of cardiovascular death, heart attack or stroke which was unchanged (5.4 per cent/year in each group), but this composite plus heart failure hospitalization tended to be non-significantly lower (7.3 per cent/year irbesartan vs. 7.7 per cent/year placebo). The latter difference was due to a significant reduction in hospitalizations for heart failure (2.7 per cent/year irbesartan vs. 3.2 per cent/year placebo) by 14 per cent. There was also a significant reduction in stroke, non-central-nervous-system embolism, and transient ischemic attacks (2.9 per cent/year irbesartan vs. 3.4 per cent/year placebo) by 13 per cent. There was a significant reduction in hospital admissions and the number of days in hospital for cardiovascular reasons. Irbesartan was similarly tolerated compared to placebo.

"The modest BP lowering with irbesartan in the trial likely occurred because patients were already receiving several BP-lowering drugs before entering the trial, and this was intensified to a greater extent in the placebo group during the trial," said Dr. Stuart Connolly, a professor

of medicine in the Michael G. DeGroote School of Medicine at McMaster University, a member of the Population Health Research Institute and the principal investigator of the trial.

"When one considers that the difference in systolic BP between groups was less than 3 mm Hg, the 13 per cent to 14 per cent relative risk reduction in heart failure and cerebrovascular and other embolic events is clinically important, and suggests that more aggressive BP lowering may have an even larger benefit."

"By demonstrating the reduction in cardiovascular hospitalizations, the ACTIVE I study highlights the importance of multiple approaches in tackling the total burden of disease in patients with AF," said Dr. Marc Pfeffer, Dzau Professor of Medicine, Harvard University Medical School at the Brigham and Women's Hospital in Boston. Dr. Pfeffer is the U.S. National Coordinator and a member of the ACTIVE Executive Committee.

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