Clinicians urged to consider spironolactone in HFPEF despite TOPCAT results

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Clinicians have been urged to consider using spironolactone in their patients with heart failure and preserved ejection fraction (HFPEF) after a post-hoc analysis of the TOPCAT trial showed benefit in patients from the Americas.

The research was presented today at the Heart Failure Congress 2014 in Athens, Greece. The Congress is the main annual meeting of the Heart Failure Association of the European Society of Cardiology.

Professor Bertram Pitt said: "We've had many studies showing that ACE inhibitors, angiotensin receptor blockers, beta blockers and mineralocorticoid receptor blockers reduce mortality and hospitalisations in patients with heart failure and reduced ejection fraction (HFREF). But no studies have found a benefit of these medications in HFPEF patients."

He added: "The results of TOPCAT are complicated. The trial failed to meet its primary endpoint but post-hoc analysis has shown that spironolactone was beneficial in patients from the Americas. I think individual clinicians around the world need to look at the data and decide for themselves. If I was a clinician I would use spironolactone in my patients with HFPEF."

TOPCAT randomised 3445 patients with HFPEF to receive spironolactone, a mineralocorticoid receptor antagonist, at a dose of 15-45mg per day or placebo on top of usual care. Patients were recruited

from 270 medical centres in 6 countries. Nearly half of the patients were from Russia and Georgia, and the remainder were from the Americas which included Canada, the US, Argentina and Brazil.

After a mean follow up of 3.3 years, the primary endpoint - which was a composite of reduction in cardiovascular mortality, resuscitated cardiac arrest and hospitalisation for heart failure - was reduced but was not reduced significantly.1 It occurred in 320 of 1722 patients in the spironolactone group (18.6%) and 351 of 1723 patients in the placebo group (20.4%) (hazard ratio [HR]=0.89; 95% confidence interval [CI]=0.77 to 1.04; p=0.14).

One component of the primary endpoint, time to heart failure hospitalisations, was reduced significantly. It occurred in 12.0% patients in the spironolactone group and 14.2% in the placebo group (HR=0.83; 95% CI=0.69 to 0.99; p=0.04).

In patients treated with spironolactone there was an associated increase in serum creatinine and the rate of hyperkalemia doubled. But Professor Pitt said: "These alterations did not have adverse affects. There were no deaths attributable to hyperkalemia and no increase in renal failure."

He continued: "The overall results of the trial were negative in that the primary endpoint was not reduced significantly. But when we examine the results by geographical region they tell a different story."

Post-hoc analysis showed that patients recruited from Russia and Georgia had an extremely low placebo event rate that was not compatible with prior HFPEF studies. In contrast, patients from the Americas had an increased placebo event rate that was compatible with previous studies. In the Americas there was a significant reduction in the primary endpoint, including cardiovascular mortality and hospitalisations for heart failure.

Professor Pitt said: "The low placebo event rate in patients from Russia and Georgia was equal to that of patients with hypertension or another cardiovascular risk factor, not heart failure. We suspect that many of the patients from these countries did not have HFPEF, but had shortness of breath due to obesity or lung disease and were misclassified as heart failure. Whereas patients in the Americas did have HFPEF."

He concluded: "My view is that spironolactone works very well in HFPEF patients and our results were diluted by the inclusion of patients without HFPEF. Clinicians should look at our data and make their own decision about whether to offer spironolactone to their HFPEF patients. I would certainly use it given the lack of other treatments. Provided clinicians monitor potassium and renal function, the results of the TOPCAT trial show that spironolactone can be given safely to patients with HFPEF."

Provided by European Society of Cardiology

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