Comparative amiodarone, dronedarone benefits in AF remain uncertain

MedWire News: Indirect comparative meta-analysis results indicate that amiodarone is more effective than dronedarone for maintenance of sinus rhythm in patients with atrial fibrillation (AF), but is associated with more adverse effects.

"For every 1000 patients treated with dronedarone instead of amiodarone, we estimate approximately 228 more recurrences of AF in exchange for 9.6 fewer deaths and 62 fewer adverse events requiring discontinuation of drug," report the authors, led by Jonathan Piccini (Duke University Medical Center, Durham, North Carolina, USA).

The researchers analyzed four placebo-controlled trials each for dronedarone and amiodarone and one trial comparing the two drugs head to head.

"The clinical decision to prescribe drugs for rhythm management hinges on estimates of their net clinical benefit," they explain, but "few direct comparisons of dronedarone and amiodarone exist, although each drug has been evaluated extensively against placebo."

As reported in the *Journal of the American College of Cardiology*, according to random-effects modeling amiodarone reduced recurrent AF significantly compared with placebo (odds ratio [OR]=0.12) whereas dronedarone did not (OR=0.79).

Normal logistic regression modeling on data from all the trials indicated that amiodarone was superior to dronedarone at preventing recurrent AF (OR=0.49, p<0.001), ie, patients treated with amiodarone were twice as likely as those on dronedarone to remain in sinus rhythm.

But there was a trend towards increased mortality (OR=1.61, p=0.066) and a significantly greater rate of adverse events requiring drug discontinuation (OR=1.81, p<0.001) with amiodarone versus dronedarone.

"More long-term data are needed to refine these estimates and to define the optimum balance of efficacy and toxicity for patients with AF," conclude Piccini and team.

Expanding on Piccini and co-authors' admission of inherent limitations to meta-analysis data and the lack of power of available studies, Paul Chan (Mid America Heart Institute, Kansas City, Missouri, USA) and colleagues highlight in a related editorial that there are marked differences in the type and size of study populations between amiodarone and dronedarone studies, and very few data on highly symptomatic AF patients – despite elimination of symptoms often being the primary reason to attempt to restore and maintain sinus rhythm.

They write: "Although this study... does raise provocative questions regarding the effectiveness and safety of dronedarone versus amiodarone, the results are hypothesis generating and require confirmation from direct comparisons in adequately powered clinical trials.

"In the meantime, clinicians will need to balance whether the use of dronedarone, a less efficacious but possibly safer antiarrhythmic drug than amiodarone (in patients without reduced ejection fraction), is justified for their patients with AF."

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