

Spironolactone "a clear winner" for resistant hypertension

August 31 2015

In patients with poor blood pressure control despite treatment with a combination of three drugs ('resistant hypertension'), addition of the diuretic spironolactone was significantly more effective than adding other blood pressure lowering drugs, according to results of the PATHWAY-2 trial.

The Hot Line findings, presented today at ESC Congress 2015, suggest spironolactone "was a clear winner and should be first choice for the additional treatment of resistant hypertension," said investigator Bryan Williams, MD.

"These results have broad international relevance and applicability," noted Professor Williams, who is from University College London, and the British Hypertension Society Research Network.

"The PATHWAY-2 study showed that spironolactone was overwhelmingly the most effective [blood pressure](#)-lowering therapy compared to bisoprolol or doxazosin and suggest that the predominant underlying cause of resistant hypertension is sodium retention - even among patients with baseline diuretic therapy. This establishes, for the first time, a clear hierarchy for drug treatment of resistant hypertension which should influence future treatment guidelines and clinical practice globally."

Resistant hypertension is defined as uncontrolled blood pressure (BP) despite treatment with at least 3 BP-lowering medications.

Prior to PATHWAY-2 there was no strong evidence supporting recommendations for the most appropriate additional drug to control blood pressure, and "there has been a growing perception that controlling BP in resistant hypertension is beyond the reach of existing drug therapies," explained Professor Williams. "But PATHWAY-2 shows that control is possible in the majority of patients, using a drug that has been available for many decades."

While the pathogenesis of resistant hypertension is poorly understood, one hypothesis is that it could be related to sodium retention – a result of reduced diuretic doses in recent years, he said.

PATHWAY 2 examined whether additional diuretic therapy with spironolactone would be the most effective at reducing BP compared to treatment with two other antihypertensives that have different mechanisms of action: doxazosin which acts to reduce arterial resistance, and bisoprolol which acts to reduce cardiac output.

The study included patients with resistant hypertension who were already treated with maximally tolerated doses of a combination of three drugs: an ACE-inhibitor or angiotensin receptor blocker (ARB); a calcium channel blocker (CCB); and a thiazide type diuretic. "The key question was, which drug should be added to get blood pressure controlled," said Professor Williams.

Uncontrolled BP was defined as seated clinic systolic BP of 140 mmHg or more for non-diabetic patients, or 135 mmHg or more for patients with diabetes, and a home systolic BP (HSBP) 130mmHg for all patients.

In addition to their baseline BP therapy, patients were randomised to sequentially receive 12 weeks of spironolactone (25-50mg), bisoprolol (5-10mg), doxazosin (4-8mg modified release) and placebo in random

order.

Blood pressure was measured with an automated BP monitor and recorded both in the clinic as well as at home over 4 consecutive days at baseline as well as at 6 and 12 weeks of each [treatment](#) cycle.

The primary end-point was average home [systolic blood pressure](#) (HSBP) for each of the treatments, with clinic systolic BP being a secondary endpoint.

In 314 patients, spironolactone had superior HSBP control compared to placebo (a reduction of 8.70 mmHg, P

Citation: Spironolactone "a clear winner" for resistant hypertension (2015, August 31) retrieved 11 May 2024 from <https://medicalxpress.com/news/2015-08-spironolactone-winner-resistant-hypertension.html>

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