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PRESS RELEASE

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50-year old drug could revolutionise blood pressure treatment

PATHWAY-2 Trial

A drug that has been used for over 50 years as a diuretic could revolutionise treatment of resistant hypertension, according to research published today in the Lancet.

In as many as 10% of patients with high blood pressure it is difficult to control blood pressure even when 3 or more drugs are used together. These patients have what doctors call "resistant hypertension" and are known to be at particularly high risk of stroke and heart attack.

Now British researchers have found that adding the drug spironolactone, which was first developed in 1959 as a diuretic, is substantially more effective than other blood pressure lowering drugs at lowering blood pressure in patients with resistant hypertension.

Results of the study PATHWAY-2, funded by the British Heart Foundation (BHF), are likely to change guidelines and clinical practice across the world and to influence the treatment of some millions of people, researchers say.

The study found that the drug spironolactone controlled 60% of previously uncontrolled patients with resistant hypertension and was three times more likely to do this than other commonly used blood pressure lowering drugs.

Lead author and NIHR University College London Hospitals Biomedical Research Centre Director Professor Bryan Williams said: 'The results of the study offer a spectacularly cost-effective approach to a previously intractable problem. These are some of the most difficult to treat patients with high blood pressure and we have identified a very effective treatment that is both cheap and readily available world-wide. This has the potential to influence the treatment and improve the outcome, for over 100 million people with this condition globally."

Professor Morris Brown, University of Cambridge, who with Professor Williams and Professor Tom MacDonald of University of Dundee, led the PATHWAY programme of trials undertaken by the British Hypertension Society Research Network, said the findings showed spironolactone to be "outstandingly superior to alternative drugs, and that it should be first choice for the treatment of resistant hypertension".

Prior to PATHWAY-2, there was no strong evidence to help doctors decide on the most appropriate drug to use for patients with resistant hypertension, and "there has been a growing perception that controlling BP in resistant hypertension is beyond the reach of existing drug therapies and we have shown that to be wrong," explained Professor Williams.

Professor Peter Weissberg, Medical Director at the BHF, said: "Together these clinical trials show that inexpensive drugs that have been around for a long time are successful in treating high blood pressure. As these drugs are already used in clinical practice they should quickly be taken up and used to better manage patients with high blood pressure, who appeared resistant to standard medications."

Results of the study also suggest that the predominant underlying cause of resistant hypertension may be salt retention – partly a result of reduced diuretic doses in recent years, and partly a response to the adrenal hormone, aldosterone.

The study looked at patients with resistant hypertension who were already being treated according to current guidelines and what happened when they were given an additional drug. The study examined whether additional diuretic therapy with spironolactone would be the most effective at reducing blood pressure 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.

Overall, almost three quarters of patients with uncontrolled blood pressure saw a major improvement in their blood pressure on spironolactone, with almost 60% meeting a stringent measure of blood pressure control ($P<0.001$). Spironolactone was the best drug at lowering blood pressure in 60%, whereas bisoprolol and doxazosin where the best drug in only 17% and 18% respectively.

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.

This trial, and PATHWAY-3, in press in Lancet Diabetes and Endocrinology, are part of the PATHWAY programme of trials in Hypertension undertaken by academic investigators within the British Hypertension Society, led by Professor Morris Brown of the University of Cambridge, Professor Williams of University College London, and Professor Tom MacDonald of the University of Dundee. The other principal investigators and sites are Professor Mark Caulfield, Queen Mary University London; Professor Kennedy Cruickshank, King's College London; Professor Ian Ford, Professor Gordon McInnes and Professor Sandosh Padmanabhan, University of Glasgow; Dr Isla Mackenzie University of Dundee; Professor David Webb University of Edinburgh and Professor Peter Sever, Imperial College London.

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The British Hypertension Society provides a medical and scientific research forum to enable sharing of cutting edge research in order to understand the origin of high blood pressure and improve its treatment.