

Two-drug combos using popular calcium channel blocker show superiority in lowering BP

March 18 2019

In the largest randomized controlled trial of treatment for high blood pressure ever conducted in sub-Saharan Africa, two frontline two-drug combinations that included the long-acting calcium channel blocker, amlodipine, were able to drive down blood pressure levels more than a third two-drug combination that did not include amlodipine, according to research presented at the American College of Cardiology's 68th Annual Scientific Session. Nearly half of adults in Africa have high blood pressure, a higher proportion than on any other continent, according to the World Health Organization. Yet many receive either no treatment or ineffective treatment, leaving them at high risk for complications such as heart disease, stroke and kidney disease.

"In [black patients](#) in sub-Saharan Africa, the combination regimens amlodipine plus hydrochlorothiazide (A/H) and amlodipine plus perindopril (A/P) were significantly more effective than perindopril plus hydrochlorothiazide (P/H) at reducing average 24-hour ambulatory systolic [blood pressure](#) (ASBP) over a six-month period, the study's primary endpoint," said Dike Ojji, MD, of the College of Health Sciences, University of Abuja, Nigeria, and the study's lead author.

These two therapies lowered ASBP by 18.1 mm HG and 17.1 mm Hg respectively over a six-month period.

Studies have shown that many patients with [high blood pressure](#) need to

take at least two medications to bring their blood pressure down to a healthy level. Among Africans, 80 to 90 percent of patients need at least two medications to attain blood pressure control, Ojji said. Yet the relative effectiveness of commonly prescribed two-drug combinations in the black African population was not known.

The current trial, with the acronym CREOLE, was designed to help answer this question, he said.

In combination therapy, drugs that work in different ways to reduce blood pressure are combined. For example, amlodipine is a [calcium channel blocker](#), which helps blood vessels relax by blocking calcium from entering muscle cells in the heart and blood vessels.

Hydrochlorothiazide is a diuretic, or "water pill," which works by flushing excess water and salt from the body via urine. Perindopril is an ACE inhibitor, which helps [blood vessels](#) relax by blocking a hormone that causes them to narrow.

In the trial, 728 patients with blood pressure of at least 140/90 mm Hg were randomly assigned to receive one of the three two-drug combinations (A/H, A/P or P/H) for six months. The patients were from six countries in sub-Saharan Africa (Cameroon, Kenya, Mozambique, Nigeria, South Africa and Uganda). Their average age was 51 years and 63 percent were women. Two-thirds of the patients were being treated for high blood pressure for the first time; the remaining one-third still had high blood pressure despite treatment with a single medication.

Although the study medications are usually distinguishable by their different shapes and colors, for the study they were packaged so that, to the extent possible, patients were blinded to which drugs they were taking. The investigators were also blinded to which medications patients received.

Participants' 24-hour ASBP was measured when they enrolled in the study and at the end of the six-month study period. ASBP is a relatively new technique in which a small device attached to the body measures blood pressure at 15- or 30-minute intervals around the clock for 24 to 48 hours. Because [blood pressure levels](#) fluctuate throughout the day and night, ambulatory monitoring provides a more accurate reading than a single measurement of blood pressure taken in a clinician's office.

Patients made follow-up clinic visits every two months during the study and were monitored by phone in between visits. They brought their medications with them to clinic visits so that their pills could be counted to verify that they were taking the pills as directed.

The study's primary endpoint was the change in 24-hour ASBP during that six-month period. Secondary endpoints included change in daytime ASBP, nighttime ASBP and blood pressure readings in the clinic. At six months, study-entry and six-month ASBP readings were available for 621 patients.

At study entry, patients' average 24-hour ASBP was 146.7 mm Hg. Over the six-month study period, the average reduction in 24-hour ASBP was 3.14 mm Hg greater for patients assigned to A/H and 3 mm Hg greater for patients assigned to A/P, compared with patients assigned to P/H. The results were statistically significant for both A/H compared with P/H and A/P compared with P/H. At the six-month mark, patients' average 24-hour systolic blood pressure was 128.0 mm Hg.

For the secondary endpoint of blood pressure readings in the clinic, the average reduction was 7.15 mm Hg greater for patients assigned to A/H and 5.55 mm Hg greater for patients assigned to A/P, compared with patients assigned to P/H.

About 5 percent of the [patients](#) assigned to A/H experienced a drop in

[blood](#) levels of potassium to below the normal range, Ojji said. Patients taking this combination regimen should have their potassium levels checked frequently and may need to consume more potassium-rich foods such as vegetables and bananas, he said.

More information: Dike B. Ojji et al, Comparison of Dual Therapies for Lowering Blood Pressure in Black Africans, *New England Journal of Medicine* (2019). [DOI: 10.1056/NEJMoa1901113](https://doi.org/10.1056/NEJMoa1901113)

Provided by American College of Cardiology

Citation: Two-drug combos using popular calcium channel blocker show superiority in lowering BP (2019, March 18) retrieved 18 April 2024 from <https://medicalxpress.com/news/2019-03-two-drug-combos-popular-calcium-channel.html>

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