

Clinical trial finds common diabetes medication could help with treatment-resistant hypertension

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A common diabetes medication may help some patients with treatment-resistant hypertension slightly lower their high blood pressure and lessen

their risk of heart failure events such as stroke, according to an analysis of a clinical trial [published](#) in *Circulation*.

For patients with heart failure with mildly reduced or preserved ejection fraction—a condition which leads to stiffening of the heart muscle, preventing the heart from filling with blood properly—treatment-resistant [high blood pressure](#) can increase the chances of adverse outcomes such as stroke and impaired [kidney function](#).

Nearly 6.5 million Americans over the age of 20 have some form of heart failure, according to estimates from the Heart Failure Society of America, and patients with mildly reduced or preserved ejection fraction make up at least 50% of all heart failure patients.

Because treatment-resistant high [blood pressure](#) increases the risk of stroke and death in patients with heart failure with mildly reduced or preserved ejection fraction, investigators wanted to understand the effects the drug dapagliflozin had on this particular subset of patients, said Sanjiv Shah, '00 MD, the Neil J. Stone, MD, Professor and director of the Center for Deep Phenotyping and Precision Therapeutics in the Institute for Artificial Intelligence in Medicine, who was a co-author of the study.

"Patients with apparent treatment-resistant hypertension are a challenging group of patients who have heart failure, especially heart failure with preserved or mildly reduced ejection fraction," Shah said. "Oftentimes these patients are fluid overloaded, so the first thing we usually do is get them on a diuretic. Oftentimes that is not enough, and they need multiple [blood pressure medications](#). In this trial, we wanted to see what happened to this group of patients when we gave them dapagliflozin, an SGLT2 inhibitor."

In the current study, the investigators analyzed the results of a previous

clinical trial they conducted examining patients with heart failure with preserved ejection fraction and the effects of the diabetes medication dapagliflozin. The drug works by blocking the absorption of glucose in the kidney, resulting in greater loss of sodium and water in the urine, thereby treating the dangerous fluid retention that occurs in heart failure patients.

Among the 6,263 patients with heart failure with mildly reduced or preserved [ejection fraction](#) who participated in the original clinical trial, 718 had treatment-resistant high blood pressure, which was still uncontrolled despite the use of three [antihypertensive drugs](#) including a diuretic.

Compared to peers who had healthy blood pressure or blood pressure that was controlled with a medication, patients with treatment-resistant high blood pressure experienced the greatest reduction in the rate of cardiovascular events while taking dapagliflozin, according to the study.

Although dapagliflozin slightly reduced [systolic blood pressure](#), according to the study, it did not lead to a significant number of participants with treatment-resistant high blood pressure attaining healthy blood pressure while on the drug.

The findings underscore the need for more research to understand which combinations of drugs benefit heart failure patients with treatment-resistant high blood pressure, Shah said.

"We were hoping that by adding an SGLT2 inhibitor dapagliflozin, we would basically convert these treatment-resistant hypertension patients into non-resistant hypertension, meaning they were now on a fourth drug, and they would be treated," Shah said. "Overall, dapagliflozin only modestly reduced blood pressure—by 1 to 3 millimeters mercury. However, despite only slight reduction in blood pressure, dapagliflozin

was still associated with improved outcomes, highlighting the importance of its use in [heart failure patients](#)."

Moving forward, physicians may need to tailor drug combinations for each individual patient in order to address treatment-resistant high [blood pressure](#), Shah said.

"I think in the future we are going to see combinations of SGLT2 inhibitors with other drugs," Shah said. "We know that in combination drugs where two or three classes of drugs are put in a single pill, adherence is better and tolerability seems to be better. These so-called 'polypills' will be a really interesting concept in the future, where we are combining evidence-based drugs for [heart failure](#) with preserved injection fraction to enhance adherence and efficacy of these medications."

More information: John W. Ostrominski et al, Dapagliflozin and Apparent Treatment-Resistant Hypertension in Heart Failure With Mildly Reduced or Preserved Ejection Fraction: The DELIVER Trial, *Circulation* (2023). [DOI: 10.1161/CIRCULATIONAHA.123.065254](https://doi.org/10.1161/CIRCULATIONAHA.123.065254)

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