Among effective antihypertensive drugs, less popular choice is slightly safer

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Two types of drugs that are recommended as a first treatment for patients with high blood pressure were found equally effective in improving cardiovascular outcomes, but the more popular type causes

slightly more side effects, finds a multinational observational study led by researchers at Columbia University Vagelos College of Physicians and Surgeons.

The study, which analyzed claims and electronic health data from millions of patients worldwide, is the largest to compare the safety and efficacy of angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs), two commonly prescribed antihypertensive drugs.

"Physicians in the United States and Europe overwhelmingly prescribe ACE inhibitors, simply because the drugs have been around longer and tend to be less expensive than ARBs," says George Hripcsak, MD, the Vivian Beaumont Allen Professor and chair of biomedical informatics at Columbia University Vagelos College of Physicians and Surgeons and senior author of the study.

"But our study shows that ARBs are associated with fewer side effects than ACE inhibitors. The study focused on first-time users of these drugs. If you're just starting drug therapy for hypertension, you might consider trying an ARB first. If you're already taking an ACE inhibitor and you're not having any side effects, there is nothing that we found that would indicate a need for a change."

The study was published online in *Hypertension*.

Narrowing Down Choices

Once a physician decides to prescribe medication to control a patient's high blood pressure, the next decision—which one to choose—is complicated.

"U.S. and European hypertension guidelines list 30 medications from

five different drug classes as possible choices, yet there are very few head-to-head studies to help physicians determine which ones are better," Hripcsak says. "In our research, we are trying to fill in this information gap with real-world observational data."

ACE inhibitors and ARBs are among the choices, and they have a similar mechanism of action. Both reduce the risk of stroke and heart attacks, though it's known that ACE inhibitors are associated with increased risk of cough and angioedema (severe swelling in the face and airways).

"We wanted to see if there were any surprises—were both drug classes equally effective, and were ARBs producing any unexpected side effects when used in the real world?" Hripcsak says. "We're unlikely to see head-to-head clinical trials comparing the two since we are reasonably sure that both are effective."

Electronic Health Records Provide Answer

The researchers instead turned to large databases to answer their questions. They analyzed insurance claims and electronic health records from approximately 3 million patients in Europe, Korea, and the United States who were starting antihypertensive treatment with either an ACE inhibitor or an ARB.

Data from electronic health records and insurance claims are challenging to use in research. They can be inaccurate, incomplete, and contain information that biases the results. So the researchers employed a variety of cutting-edge mathematical techniques developed by the Observational Health Data Science and Informatics (OHDSI) collaborative network to dramatically reduce bias and balance the two treatment groups as if they had been enrolled in a prospective study.

Using this approach, the researchers tracked four cardiovascular outcomes—heart attack, heart failure, stroke, and sudden cardiac death—and 51 adverse events in patients after they started antihypertensive treatment.

The researchers found that the vast majority of patients—2.3 million—were prescribed an ACE inhibitor. There were no significant differences between the two drug classes in reducing the risk of major cardiovascular complications in people with hypertension. Patients taking ACE inhibitors had a higher risk of cough and angioedema, but the study also found they had a slightly higher risk of pancreatitis and gastrointestinal bleeding.

"Our study largely confirmed that both antihypertensive drug classes are similarly effective, though ARBs may be a little safer than ACE inhibitors," Hripcsak says. "This provides that extra bit of evidence that may make physicians feel more comfortable about prescribing ARBs versus ACE inhibitors when initiating monotherapy for patients with hypertension. And it shows that large-scale observational studies such as this can offer important insight in choosing among different treatment options in the absence of large randomized clinical trials."

The study, titled "Comparative first-line effectiveness and safety of angiotensin converting enzyme inhibitors and angiotensin receptor blockers: a multinational cohort study," was published online July 26, 2021, in *Hypertension*.

More information: "Comparative first-line effectiveness and safety of angiotensin converting enzyme inhibitors and angiotensin receptor blockers: a multinational cohort study," *Hypertension* (2021). dx.doi.org/10.1161/HYPERTENSIONAHA.120.16667