Clopidogrel superior to aspirin for long-term post-stent maintenance

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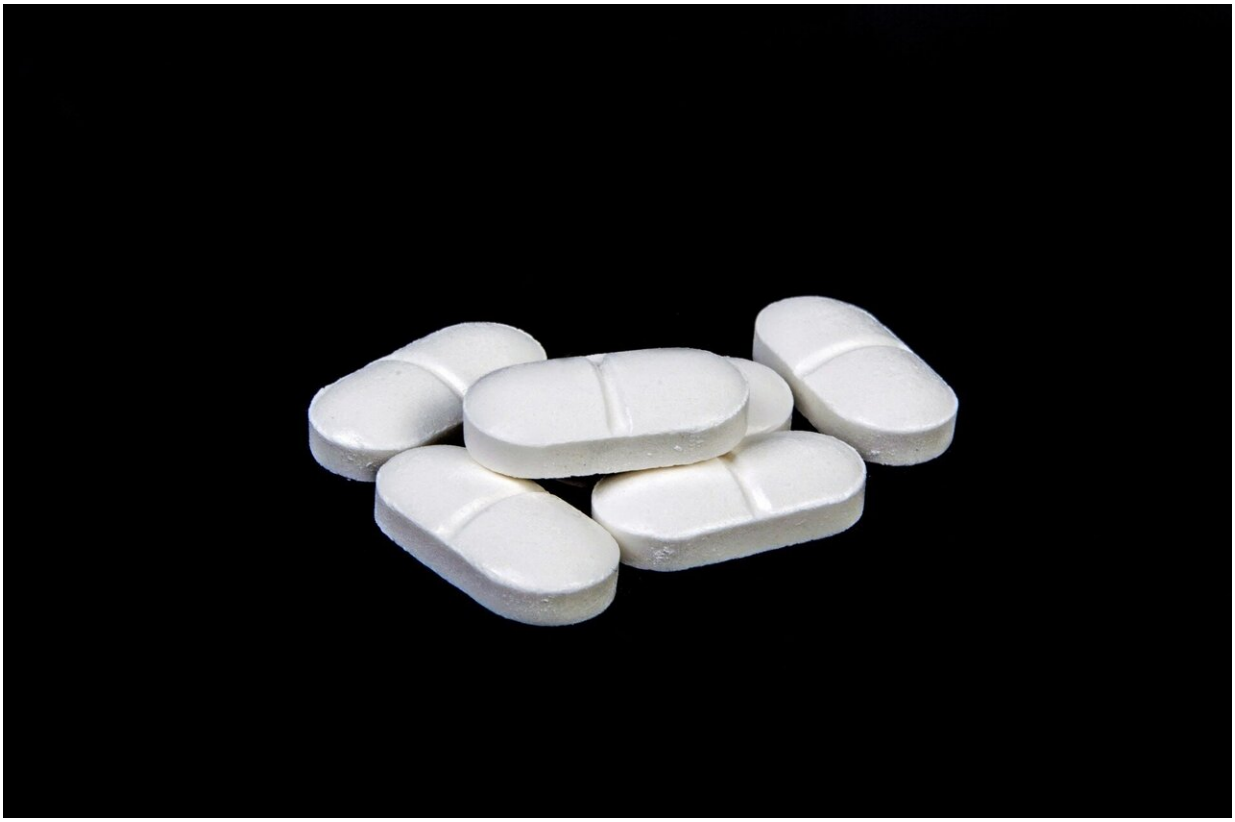

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Clopidogrel outperformed aspirin in what is believed to be the first and largest randomized trial to compare the effectiveness of the two antiplatelet drugs as long-term maintenance therapy for patients who had

no adverse events after one year of dual antiplatelet therapy (DAPT) following the insertion of a coronary stent. After two years of follow-up, chronic maintenance therapy with clopidogrel resulted in a 30% reduction in deaths, heart attacks, strokes or major bleeding events, according to research presented at the American College of Cardiology's 70th Annual Scientific Session.

"These data confirm our working hypothesis that long-term maintenance antiplatelet monotherapy with clopidogrel produces better outcomes than aspirin in patients who are adverse event-free at one year after coronary stenting," said Hyo-Soo Kim, MD, Ph.D., professor of internal medicine at Seoul National University Hospital in South Korea and lead author of the study.

The trial met its primary endpoint, a composite of death from any cause, heart attack, stroke or a major bleeding event within two years of study entry, which occurred in 5.7% of patients assigned to clopidogrel and 7.7% of those assigned to aspirin.

Ischemic heart disease is an umbrella term for problems caused by insufficient blood flow to the heart, such as heart attacks and unstable angina. Stenting, also known as coronary angioplasty or percutaneous coronary intervention, is a minimally invasive procedure in which a flexible tube (catheter) is threaded through an artery under local anesthesia. At the site of an arterial blockage, a tiny balloon at the tip of the catheter is inflated to unblock the artery, and a stent—a tiny mesh tube coated with medication—is inserted to prop the coronary artery open and restore blood flow to the heart.

Blood cells known as platelets help the blood to clot, and both clopidogrel and aspirin stop platelets from clotting. Current treatment guidelines recommend a DAPT regimen of two antiplatelet drugs for six to 12 months after the insertion of a coronary stent to prevent blood clots

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"However, the optimal single antiplatelet agent for long-term maintenance therapy beyond the duration of DAPT has been unclear," Kim said. He added that in clinical practice, physicians may maintain patients on DAPT for as long as 18 months, depending on the patients' level of risk for clotting.

This trial, known as HOST-EXAM (EXtended Antiplatelet Monotherapy), enrolled 5,436 patients who had received a coronary stent. Patients' average age was 63 years; 75% were men, 34% had diabetes and 13% had chronic kidney disease. After completing between six and 18 months of DAPT without experiencing any adverse events, patients were randomly assigned to receive single-agent maintenance therapy with either clopidogrel or aspirin.

In addition to the primary endpoint, researchers also separated out blood-clotting events (death, heart attack, hospital readmission due to acute coronary syndrome, or a blood clot in the stent) from all bleeding events and analyzed them as secondary endpoints. They found that blood-clotting events occurred in 3.8% of the patients who took clopidogrel compared with 5.6% of those who took aspirin; bleeding events were seen in 2.3% of patients in the clopidogrel group versus 3.3% of those in the aspirin group. All of the differences between the groups were statistically significant.

"These results confirm that clopidogrel is superior to aspirin at reducing the incidence of blood-clotting events," Kim said. "What is interesting is that clopidogrel also performed better than aspirin at reducing bleeding events. Such findings that one antiplatelet agent is better than the other in reducing both clotting and bleeding events have been observed in other studies comparing different antiplatelet regimens, suggesting that thrombotic and bleeding events are tightly associated with each other.

For example, when patients experience bleeding, they stop the antiplatelet agents leading [them to experience] thrombotic events."

Kim said that the results apply only to patients who had completed between six and 18 months of DAPT without any adverse events.

"It may be difficult to directly extrapolate our results to patients who received DAPT for a shorter period, such as one or three months," he said. "However, our results may be useful in helping physicians to select antiplatelet monotherapy for patients who are in the chronic stable phase after coronary stenting."

The two years of patient follow-up in the HOST-EXAM trial is longer than that of many previous trials comparing antiplatelet drug regimens in patients who have received a coronary stent, Kim said. He and his colleagues plan to continue their follow-up for a total of five years to gain further insights into the long-term benefits and trade-offs of clopidogrel compared with aspirin. Because the daily cost of clopidogrel is higher than that of aspirin, Kim said, he and his team are also planning a follow-up study that will examine the cost-effectiveness of the two medications.

Another limitation is that the trial was not blinded, meaning that both patients and their doctors knew which drug patients were receiving. Also, the total number of reported adverse events in both groups was lower than the investigators had expected when they designed the trial, which suggests that adverse events could have been under-reported. However, Kim said he believes the main reason for the lower-than-expected rate of adverse events was not under-reporting but the quality of care that evolved over the seven-year study period.

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