Aspirin Resistance Attributed to Noncompliance

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ATLANTA — Noncompliance is the main cause of aspirin resistance, according to investigators who studied aspirin response in 230 people, most of whom had a history of myocardial infarction.

The study initially classified up to 30% of the participants as aspirin resistant, but in the end, only 4% of 185 people in whom aspirin response was measured met a conservative definition of aspirin resistance. These seven patients were determined to have a low response to aspirin. One person violated the study's protocols by taking a nonaspirin nonsteroidal anti-inflammatory drug (NANSAID) that would have interfered with aspirin's effects.

Among participants who complied with the protocol, aspirin responses were normally distributed, Dr. Kenneth A. Schwartz reported at the annual meeting of the American Society of Hematology. No difference was seen between those with a history of MI and those in a control group.

"In my way of thinking, there are no people other than NANSAID people that you can label as truly aspirin resistant based on genetics or some other prior inability to respond to aspirin," Dr. Schwartz, professor of medicine, Michigan State University, East Lansing, said in an interview.

Physicians should focus on compliance rather than resistance, he said, recommending that patients be tested for aspirin use when they appear to be resistant. "We found about 30% of patients could be labeled as aspirin resistant, and 90% of them [62 of 69 patients] were noncompliant."

Dr. Schwartz and his colleagues started with 230 evaluable individuals, all of whom were told not to take aspirin for 7 days. After that period, they removed 45 patients from the study because they were not compliant with the protocol during the withdrawal period.

This left 185 participants—146 with a history of MI and 39 normal controls—in whom aspirin response was measured with platelet prostaglandin agonist (PPA) stimulated light aggregometry. The participants' average age was 61 years, and 63% were men. Blood was drawn twice: immediately after the 7-day washout period, and then 2 hours after a nurse observed each participant ingesting 365 mg of aspirin.

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"We were sure they were off aspirin because we checked with arachidonic acid," Dr. Schwartz said. "And we were sure that they were on aspirin … because we watched them take the aspirin. And that's why we got a nice normal curve."

Arachidonic acid testing reveals whether a patient is taking aspirin, which inhibits cyclo-oxygenase-1–mediated events leading to platelet aggregation. The researchers used PPA-stimulated light aggregometry to measure the extent of aspirin-induced platelet inhibition. To define net aspirin response, they subtracted the slope of each patient's post-aspirin PPA light aggregation curve from the curve recorded when the patient was aspirin free.

The seven low responders had a decrease that was less than one standard deviation, but the investigators suggested they might not be a distinct population but the bottom of a normal bell-shaped distribution curve. "If there was a separate group of patients that were aspirin resistant, this would show a subgroup in which there was a poor response, and we don't see that," he said.

In an earlier phase of the study, he said, arachidonic acid failed to show the expected aspirin inhibition in 17 of 192 heart attack patients who had been prescribed aspirin. All but one showed aspirin inhibition when they were retested 2 hours after being observed taking aspirin, however. The patient admitted taking a NANSAID in violation of the protocol, leaving the investigators to conclude that the other 16 were not aspirin resistant but rather were noncompliant with their prescribed aspirin use.

Dr. Schwartz said patients should be counseled about the importance of aspirin to their survival. "If you don't get your aspirin, you don't get your benefit," he said. "Aspirin is one of the most effective drugs we have in terms of platelet inhibition." ■