Aspirin Resistance Attributed to Noncompliance

BY JANE SALODOF MACNEIL Senior Editor

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 alongside his poster.

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

Dr. Schwartz and his colleagues started with 230 evaluable individuals, all of whom were told not to take aspirin for 7 days. After the 7 days, they removed 45 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.

"These patients were very special because 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 can reveal whether a patient is taking aspirin, which inhibits cyclo-oxygenase-1-mediated events leading to platelet aggregation. A relatively new test, PPA-stimulated light aggregometry allowed the investigators to measure the extent of aspirin-induced platelet inhibition. To define net aspirin response, they subtracted the slope of each patient's postaspirin PPA light aggregation curve from the curve recorded when the patient was aspirin free. While the seven low responders had a decrease that was less than one standard deviation, the investigators suggested they might not be a distinct population but the bottom of a normal bell-shape 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 1 patient admitted to 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 that patients should be counseled about the importance of aspirin to their survival. "Aspirin is one of the most effective drugs we have in terms of platelet inhibition."

Childhood Trauma Boosts Risk of CHD, Depression

BY MITCHEL L. ZOLER Philadelphia Bureau

VIENNA — Childhood trauma was an independent predictor of coronary heart disease and major depression later in life in a study with 360 men.

"Childhood trauma can have important consequences, but it is a risk factor that physicians don't usually think about," Dr. Viola Vaccarino said while presenting a poster at the annual congress of the European Society of Cardiology.

"Once a person is identified with a history of childhood trauma, that person needs to be monitored very closely. Our data [suggest] that childhood trauma may be a key history to ask about," said Dr. Vaccarino, a professor of medicine and epidemiology at Emory University, Atlanta.

The study by Dr. Vaccarino and her associates used 360 male twins (180 pairs, either mono- or dizygotic) who were born in 1946-1956 and were enrolled in the Vietnam Era Twin Registry. The participants were all interviewed at Emory University. They were assessed using the Early Trauma Inventory (ETI), a measure of traumatic events occurring before age 18 years, and the Late Trauma Inventory (LTI), a measure of traumatic events that occur when a person is aged 18 years or older. Physical health was assessed by examination, and mental health was assessed with the Structured Clinical Interview for Psychiatric Disorders. In all, 33 participants were diagnosed with coronary heart disease (CHD), 82 were diagnosed with major depressive disorder, and 23 had posttraumatic stress disorder.

The participants were divided into quartiles based on their ETI scores.

The analysis showed that the men in the three lowest ETI quartiles had a 6% prevalence of CHD compared with an 18% rate in the quartile with the highest ETI score. When adjusted for age and smoking history, the men in the highest quartile for childhood trauma had about a twofold increased rate of CHD, compared with men with lower ETI scores, a statistically significant difference.

A second analysis showed that men in the quartile with the greatest childhood trauma were also about twice as likely to have major depression (36%), compared with men with lower ETI scores (18%), also a significant difference, said Dr. Vaccarino, who is also director of EPICORE (Emory Program in Cardiovascular Outcomes Research and Epidemiology).

Initially, an excess of CHD and depression was also seen in men who had high scores on the LTI. But when the LTI analysis was adjusted for the prevalence of early trauma, the link between the LTI score and CHD and depression disappeared. In contrast, a strong link was also seen between high LTI scores and posttraumatic stress disorder, but this link was not affected by adjustment for ETI scores.

Childhood trauma can occur in the form of physical abuse, emotional abuse, sexual abuse, or general trauma, which is caused by events such as earthquakes and car accidents.

These findings suggest that primary care physicians should routinely ask patients about their trauma exposures as children. They may even want to administer the ETI, which has recently been streamlined to a single-page questionnaire, Dr. Vaccarino suggested in an interview.

Implantable Cardioverter Defibrillators Can Trigger Psychiatric Sequelae

VIENNA — Psychiatric assessment of 82 Turkish patients who had received implantable cardioverter defibrillators showed that the recipients had a high prevalence of sexual dysfunction, posttraumatic stress disorder, major depressive disorder, panic disorder, and generalized anxiety disorder, Dr. Irem Yalug said while presenting two posters at the annual congress of the European Society of Cardiology.

Psychiatric assessment and counseling should be part of routine follow-up after implantable cardioverter defibrillator (ICD) placement, said Dr. Yalug, a psychiatrist at Kocaeli (Turkey) University. As part of this work-up, patients should be assessed and informed that sexual activity will not boost their risk of an ICD shock, she added.

Dr. Yalug and associates studied patients at risk for lethal ventricular arrhythmias who received ICDs for either the primary or secondary prevention of a sudden cardiac event at Kocaeli University during 2002order. (See box.) The average score on the Arizona Sexual Experience Scale was about 17, a "very high score" indicating abnormalities on a scale where 11 is at the upper level of normal, Dr. Yalug said. The traumatic event that triggered

including PTSD and major depressive dis-

The traumatic event that triggered PTSD was either a ventricular arrhythmia or the placement of the ICD. Patients also showed a high prevalence of multiple disorders. About 60% of the patients with depression also had PTSD; about 40% of those with PTSD also had depression.

"We saw a high rate of concern about sexual activity in these patients," Dr. Yalug said. "To improve quality of life and reduce anxiety, patients should be assessed and counseled about sexual activity as soon as possible after ICD placement." Avoiding sexual activity may lead to some of the other sequelae seen in this study, such as depression, she said.

-Mitchel L. Zoler

2006. The group included 69 men and 13 women, with an average age of 59 years. All patients had their ICDs for at least 3 months.

Patients were assessed using sociodemographic and psychiatric questionnaires, including the Structured Clinical Interview for DSM-IV and Arizona Sexual Experience Scale. The results

showed a high prevalence of psychiatric disorders,

Prevalence of Psychiatric Disorders After Implantable Cardioverter Defibrillator Placement 87% Sexual dysfunction Posttraumatic 43% stress disorder 28% **Major depression** 18% Panic disorder Generalized 10% anxiety disorder Obsessive-4% compulsive disorder Note: Based on a study of 82 patients with an average age of 59 years.

Note: Based on a study of 82 patients with an average age of 59 years. Source: Dr. Yalug