Acute Coronary Syndromes

Aspirin Resistance Attributed to Noncompliance

BY JANE SALODOF McNEIL
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 patients 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 (NASSAD) that would have interfered with aspirin’s effects.

Among participants who complied with the protocol, aspirin resistance was 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 NASSAD people that you can label as truly aspirin resistant,” he said. “Aspirin is one of the most effective drugs we have in terms of platelet inhibition.”

CD34+ Stem Cell Transplant Helps in Refractory Angina

By Nancy Walsh
New York Bureau

New York — Therapeutic neovascularization through the intramyocardial administration of autologous CD34+ stem cells is a promising approach in patients with refractory ischemia, Dr. Timothy D. Henry said at a conference on cell therapy and cardiovascular diseases.

Many patients with severe coronary artery disease experience persistent, disabling angina despite the use of antiangiogenic drugs and mechanical revascularization, and few good options exist for these patients at present, according to Dr. Henry, who is chief of research, Minneapolis Heart Research Foundation, Minneapolis.

Preclinical studies suggested that neovascularization is possible in chronic ischemia following the administration of autologous endothelial progenitor cells, and particularly when cells expressing the CD34+ marker were used. A pilot study has now provided evidence that this approach is safe and may result in symptomatic improvements in angina symptoms, Dr. Henry said.

The treatable group included 24 patients comprising 5 women and 19 men, whose mean age was 62 years. All had Canadian Cardiovascular Society (CCS) class III or IV angina, were not candidates for conventional revascularization, had failed on optimal medical therapy, and were on at least two antiangiogenic medications.

Initially all patients underwent a cellular mobilization with granulocyte colony-stimulating factor for 5 days, at which time leukapheresis was performed and the CD34+ fraction of mononuclear cells were isolated.

They then underwent cardiac navigation using NOGA electro-mechanical mapping and intramyocardial injection of the CD34+ cells or placebo into the ischemic zone, and were followed for 12 months.

The treatment was well tolerated, with no serious adverse events related to the cell therapy, Dr. Henry said. One patient in the placebo group developed ventricular tachycardia during the procedure, but was cardioverted successfully.

At 3 months, the number of episodes of angina per week fell from 21 to 10 in the treated group, and rose from 21 to 27 in the placebo group. By 6 months, the number of episodes per week had fallen to 9 and 16 in the treated and placebo groups, respectively (Circulation 2007;115:3167-72).

By 6 months, 90% of patients in the treated group had experienced an improvement by at least two CCS classes, as had 31% of placebo patients.

Results on single-photon emission computed tomography (SPECT) were mixed, showing some improvement at 3 months but none at 6 months, Dr. Henry said. “One of the things holding us back in treating patients with chronic refractory ischemia is the lack of a gold standard to measure myocardial blood flow,” he said.

Moreover, improvements in exercise tolerance were modest at best, increasing 0.3 minutes and 0.5 minutes in the placebo and active treatment groups at 3 months, respectively.

Previous trials of various therapies for refractory angina also have failed to demonstrate improvements in exercise tolerance. For example, in an analysis of pooled data from the Angiogenic gene therapy (AGENT) 1 and 2 studies, which evaluated the intracoronary administration of AdHFGF-4 in patients with chronic angina, there was no significant difference between the active treatment and placebo on the primary end point of change from baseline exercise time at 12 weeks. However, the incidence of angina and worsening angina was significantly less in patients receiving the gene therapy, at 18%, compared with those receiving placebo, at 25% (J. Am. Coll. Cardiol. 2007;50:1038-46).

“As far as placebo-controlled trials that show improvement in exercise time in patients with refractory angina, for angiogenesis there are none, for enhanced extracellular counterpulsation there have been none, for percutaneous transmyocardial laser revascularization there have been none, and for novel drug therapy there have been none,” Dr. Henry said.

“If you ask the patients what the problem is, they say it’s chest pain. Therefore, a larger randomized trial of CD34+ stem cells that has recently completed enrollment has, as its primary efficacy end point, frequency of angina episodes.

The study protocol calls for 150 patients aged 21-80 years who have CCS functional class III or IV refractory angina. Following the intramyocardial injection of autologous stem cells or placebo, patients will be followed up with MRI and SPECT at 6 and 12 months.

“It’s important to remember that this is a very challenging patient population, where bypass didn’t work, PCI didn’t work, and medical therapy didn’t work, and for whom we don’t have great options now.Will CD34+ therapy be a better option? Certainly the phase I trial was suggestive, and we’re excited about seeing the results of the phase II trial,” said Dr. Henry, who is a consultant to Baxter Healthcare, the study sponsor.