Gene Variant Protects Black Heart Failure Patients

By Ed Edelson
HealthDay Reporter
Monday, April 21, 2008; 12:00 AM

MONDAY, April 21 (HealthDay News) --
Researchers have discovered a gene variant carried by about 40 percent of blacks that protects them after heart failure as much as widely used beta blocker drugs do.

The finding explains the puzzling results reported in trials of beta blocker therapy in black people, said Dr. Stephen B. Liggett, a professor of medicine and physiology at the University of Maryland, and co-author of a report in the April 20 online issue of Nature Medicine.

"To our knowledge, this is the first case where a genetic variant mimics the activity of a drug used to treat a disease," Liggett said.

But Liggett predicted "further surprises" along the same lines as research on human genetic variations continues.

The finding won't have an immediate effect on treatment of heart failure, the progressive loss of ability to pump blood that affects an estimated 5 million Americans, said study co-author Dr. Gerald W. Dorn II, director of the Center for Pharmacogenomics at Washington University in St. Louis. Doctors can continue to prescribe beta blockers for people with heart failure, black or white, since the drugs have little risk, he said.

But there should be an effect on future medical practice, Dorn said. "One idea in the future of drug discovery is that we will not only need to tailor therapy for individual genetic makeup but also take genetic makeup into consideration in drug testing," he explained.

About 2 percent to 3 percent of white Americans in the total group of 2,000 who were tested carried the gene variant, he said.

The research finding was made possible by the Human Genome Project, which laid out all the more than 20,000 genes that act in humans. The researchers zeroed in on the gene pathway responsible for the activity of adrenaline, a hormone that increases cardiac output. In heart failure, the adrenal glands produce more and more adrenaline to increase blood flow. Overproduction of adrenaline causes the heart to weaken faster. Beta blockers ease the pressure on the heart by blocking adrenaline receptors in heart muscle.

The researchers looked at two genes in the adrenaline pathway, GRK2 and GRK5. They found one specific variant, designated GRK5-Leu41, that reduced the effect of adrenaline on heart cells. A study of 375 black adults with heart failure showed that among those not taking beta blockers, those with the GRK5-Leu41 variant lived twice as long as those with the more common variant. The same prolonged survival was seen in those with the normal variant who took beta blockers. Beta blocker therapy did not increase the survival of individuals with the helpful gene variant.
The same kind of genetic analysis will inevitably be extended to other drugs and other
diseases, Liggett said.

"Our idea is not to replace the physician's judgment, but to give a handle on which drugs
they might want to push to higher levels and which are less likely to be helpful for
specific individuals," he said.

More information

Heart failure and its treatment are described by the U.S. National Library of Medicine.

SOURCES: Stephen B. Liggett, M.D., professor, medicine and physiology, University of
Maryland, Baltimore; Gerald W. Dorn II, M.D., director, Center for Pharmacogenomics,
Washington University, St. Louis; April 20, 2008,Nature Medicine online