Angina drug potentially useful against heart rhythm disorders

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A recently approved angina drug may also represent a powerful new treatment for a rare hereditary syndrome that places teens at risk for sudden cardiac death, according to research presented to today at the 57th Annual Scientific Sessions of the American College of Cardiology (ACC) in Chicago.

Cardiac arrhythmias are electrical malfunctions that throw the heart out of rhythm, causing many of the 330,000 sudden cardiac deaths each year in the United States. Most fatal arrhythmias occur in aging patients when scar tissue left by a heart attack interferes with the heart's electrical system. As many as 1,000 deaths each year, however, are caused by Long QT Syndrome (LQTS), which occurs mostly in teens with otherwise healthy hearts. While rare, LQTS is yielding insights into the much more common post-heart attack arrhythmias, researchers said.

The QT interval is part of the heart’s electrical signature as recorded by an electrocardiogram (ECG). The QT represents the time it takes for the heart’s lower chambers to “reset” electrically after each heartbeat. QTc is QT corrected for heart rate, a more accurate measure. In LQTS patients, QTc reset time is prolonged, which makes the heart more susceptible to fatal arrhythmias. The condition may go unnoticed until sports, strong emotions or even loud noises knock the heart out of rhythm, causing loss of pulse and consciousness (syncope). Sudden death will then occur if the heart is not restarted with a defibrillator. Given the current state of awareness, some families have lost a second child before realizing all the children have the syndrome.

In the current, pilot study, researchers found that a drug, ranolazine (brand name Ranexa, CV Therapeutics) shortens the QT interval by about 5 percent; just enough to reduce symptoms and risks associated with one form of LQTS (LQT3-deltaKPQ). It is one of three forms of the disease that together make up 90 percent of LQTS cases. Past studies have shown that patients with angina, severe chest pain caused by inadequate blood flow to the heart, are also more likely to experience arrhythmias. Researchers got a clue that ranolazine, approved in January 2006, might influence QTc during its angina clinical trials, where it was found to have electrophysiological side effects.

“Past studies have shown that people with angina are also at risk for rhythm disorders,” said Arthur Moss, M.D., professor of Medicine in the Department of Medicine at the University of Rochester Medical Center and lead author on the ranolazine abstract. “Our study found that we may be able to treat two conditions for the price of one with this drug. Specifically, Ranolazine shortens the QTc interval and improves myocardial relaxation in patients with the LQT3 mutation.”

In a carefully controlled setting, and with informed consent, researchers gave five patients with the LQT3 mutation an 8-hour intravenous infusion of ranolazine, with ECG and ECHO evaluation before, during, and after treatment. Over the infusion period, the mean reduction in QTc from baseline was 26 +/- 3ms (p

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