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Landmark trial to evaluate cardioprotective properties of insulin

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The ability of insulin to limit heart-tissue damage during a heart attack will be tested in a landmark clinical trial led by Paresh Dandona, M.D., Ph.D., University at Buffalo Distinguished Professor in the departments of Medicine and Pharmacology and Toxicology in the UB School of Medicine and Biomedical Sciences.

Approximately 600 patients at 90 centers in the U.S. and Latin America will be recruited to participate in the two-year INTENSIVE (Intensive Insulin Therapy and Size of Infarct as a Validated Endpoint by Cardiac MRI) trial. Patients in the trial, which is funded by sanofi-aventis, will be treated with two forms of insulin -- insulin glargine and insulin glulisine.

Kaleida Health's Diabetes-Endocrine Center of Western New York, which Dandona directs, will be one of the vanguard centers. The center's research facility, located in UB's New York State Center of Excellence in Bioinformatics and Life Sciences, will serve as the core laboratory.

Richard W. Nesto, M.D., associate professor at Harvard Medical School and chair of cardiovascular medicine at Lahey Clinic Medical Center in Burlington, Mass., will be co-principal investigator, directing the trial's cardiovascular aspects.

The trial is based on a pilot study conducted by the diabetes center, which documented that insulin, used to treat and control type 1 and type 2 diabetes, was also cardioprotective.

This pilot study, published in the journal Circulation in 2004, was conducted in 32 patients receiving low-dose insulin. C-reactive protein (CRP) and serum amyloid A (SAA), two critical markers of inflammation, were reduced by 40 percent and 50 percent, respectively, during the 48 hours following a heart attack. Concentrations of three additional inflammatory factors also were significantly lower in those who received insulin, compared to those who did not.

“The markers of myocardial damage that we measured were reduced significantly,” said Dandona. “We are excited to learn more about the potential cardioprotective benefits we may discover with insulin. We think insulin will improve blood flow during a heart attack and help limit damage to heart tissue.”

Previous studies evaluating the potential benefits of insulin were confounded by glucose levels that went up simultaneously, because patients were given too much glucose.

The INTENSIVE trial will involve infusing relatively higher concentrations of insulin compared to glucose. The treatment will be tailored to those patients with diabetes who would benefit most -- patients with glucose above 140 mg/dL on admission and who have an anterior wall heart attack -- the largest type of heart attack.

“This is the first large-scale trial that will be conducted using this individually tailored treatment strategy in patients who are undergoing a coronary procedure (PCI) for their heart attack,” said Nesto.

During the two-to-three months post-heart attack period, patients will undergo an MRI, which can detect subtle change in cardiac structure and function. “The MRI technology being used in the INTENSIVE trial is at the forefront of cardiac imaging,” Nesto said.

Source: University at Buffalo