Drug treatment for Marfan syndrome looks promising

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A small study in 18 pattients assessing the effectiveness of the drug losartan for treating Marfan syndrome in children has yielded encouraging results. Reporting in the June 26 issue of *The New England Journal of Medicine*, Johns Hopkins researchers showed that losartan-a compound used for years to treat high blood pressure-slowed the enlargement of the aorta, the most life-threatening defect associated with Marfan syndrome.

"This experience increases my belief that losartan holds great promise for treating Marfan syndrome," says Harry Dietz, M.D., a professor in the McKusick-Nathans Institute of Genetic Medicine and director of the William S. Smilow Center for Marfan Syndrome Research at Hopkins. "This would be the first therapy generated by basic research that revealed the molecular mechanism of this genetic disease."

In mice engineered to contain the same genetic defect that causes Marfan syndrome, Dietz's team previously discovered that most features of the syndrome arise from excessive activity of the protein TGF-beta, a protein vital to cell growth and specialization.

Treating the mice with losartan, a drug also known to decrease TGF-beta activity, slowed, and in some cases stopped, potentially lethal enlargement of the aorta, the body's largest. Such enlargement is a key feature of Marfan syndrome.

On the basis of these findings, the Pediatric Heart Network of the

National Heart, Lung and Blood Institute at the National Institutes of Health has approved and launched a large, multicenter clinical trial of losartan for Marfan syndrome, which Dietz oversees with Ronald Lacro, M.D., director of the cardiovascular genetics clinic at Children's Hospital Boston.

Before the start of that clinical trial, physicians at Johns Hopkins felt compelled to first try losartan in a small group of children, with severe Marfan syndrome, whose aortas, which carry oxygenated blood from the hear to the resto of the body, were enlarging rapidly and unresponsive to other treatment.

"These patients had severe forms of the disease and had shown progressive aortic enlargement despite treatment with existing therapies, including beta-blockers and ACE inhibitors," says Benjamin Brooke, M.D., a research fellow in genetic medicine and surgery at Hopkins.

For the 18 patients in the small, preliminary study, the average rate of aortic enlargement before starting losartan was 3.5 millimeters in diameter per year, and after losartan treatment, just shy of a half millimeter per year. "While the response to therapy varied somewhat, it was exciting to see such a dramatic change in the majority of these patients," Brooke says.

"I am very encouraged by this initial experience, but it cannot substitute for a properly controlled clinical trial," says Dietz. "I encourage patients and families with Marfan syndrome to talk to their doctors and get involved with the current clinical trial."

Source: Johns Hopkins Medical Institutions