MedicalXpress

Cholesterol-lowering drug shrinks enlarged prostates in hamster model

October 21 2010

A cholesterol-lowering drug reduced the enlarged prostates of hamsters to the same extent as a drug commonly used to treat benign prostatic hyperplasia (BPH), report researchers at Children's Hospital Boston and their colleagues in the October issue of the Journal of Urology. Together, the drugs worked even better.

"We don't know the mechanism, but the results suggest to us that lowering cholesterol has the potential to reduce BPH in men," says senior author Keith Solomon, PhD, a biochemist, and member of the departments of Orthopaedic Surgery and Urology at Children's. "This brings up the possibility that other cholesterol lowering therapies, including exercise and diet, may prevent BPH from developing."

For unknown reasons, about half of men older than 50 (and 80 percent of men aged 80) develop BPH, most often evident as enlargement of the prostate. BPH leads to difficult urination, urgency, pain, and other symptoms that can cause significant reduction in the quality of life. In advanced stages, BPH can lead to renal failure. Standard medical and surgical treatments typically target the prostate and usually result in a reduction of symptoms but not without significant side effects in some men, Solomon said.

The study implicates circulating cholesterol in the progression of the condition and suggests a potential new strategy for prevention and treatment. The latest findings emerge from experiments with a strain of Syrian hamsters that undergo prostate enlargement naturally.

Led by first author Kristine Pelton, the team tested ezetimibe, an FDA-approved hypercholesterolemic drug (Zetia; Merck) against finasteride (Proscar, Propecia; Merck), a standard therapy for the treatment of BPH. Ezetimibe reduced prostatic enlargement in aged hamsters as effectively as finasteride and combining the two drugs worked better than either one alone.

In an unexpected finding, pathologist and co-author Dolores Di Vizio, MD, PhD, observed that finasteride caused atrophy of the hamster prostate while ezetimibe did not. "These findings provide strong evidence that the cholesterol-lowering drug inhibits BPH by a novel mechanism," said co-author Michael R. Freeman, PhD, professor of Surgery and director of urologic research at Children's Hospital.

The potentially therapeutic effect of cholesterol-lowering on enlarged prostates was pioneered 40 years earlier by co-author Carl Schaffner, PhD, professor emeritus at Rutgers University, who reported similar results in pre-clinical models using a different cholesterol-lowering drug.

"There is a lot more we want to do in the lab, with regards to studying BPH and the use of cholesterol-based therapies to control disease progression," says Solomon.

For example, the researchers want to test lower doses of ezetimibe and finasteride to examine whether the condition can be reversed with fewer side effects. They also want to assess prophylactic cholesterol lowering to determine if the enlargement can be prevented, and whether genes and proteins mediating the effect of cholesterol on the prostate can be identified. "We really want to be in the position to help conduct a clinical trial to test whether this therapy might have efficacy in human patients," Solomon said.

The study also validated the hamster strain as a good preclinical model

for testing novel BPH therapies. "The preclinical models for BPH are few, require substantial manipulation or have an unpredictable disease course," Solomon says. "The Syrian hamster model that we are now using seems particularly good for examining the role of cholesterol in prostate disease, and the testing of novel drug therapies to help alleviate symptoms. We should be able to make substantial progress in developing new treatments and in understanding the molecular mechanisms underpinning the disease using these hamsters."

More information: Ezetimibe reduces enlarged prostate in an animal model of benign prostatic hyperplasia, *Journal of Urology*, October 2010

Provided by Children's Hospital Boston