Researchers identify target to help protect kidney patients' heart health

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Blocking the receptor for proteins that constrict blood vessels reduces markers of heart-related problems in patients with chronic kidney disease (CKD), according to a study appearing in an upcoming issue of the *Journal of the American Society of Nephrology* (*JASN*). The findings might be used to improve the health of patients with CKD, who most often die from cardiovascular disease.

Patients with CKD have an increased risk of developing heart problems, in part because kidney disease can cause their arteries to stiffen. This is thought to occur due to an impaired availability of a vasodilator—nitric oxide (NO)—in the blood. The protein endothelin-1 is a vasoconstrictor and opposes the actions of NO, suggesting that drugs that block its effects may help protect CKD patients' heart health. One such drug is called sitaxentan, which blocks endothelin-1's receptor (called the ETA receptor).

Neeraj Dhaun, MD, PhD (University of Edinburgh, in Scotland) and his colleagues conducted a randomized, double-blind study in 27 patients with CKD to compare the effects of sitaxentan, nifedipine (a blood vessel relaxant), and placebo on kidney function, blood pressure, arterial stiffness, and various heart-related markers.

Among the major findings after six weeks of treatment:

- Placebo and nifedipine did not affect three markers of heart-related problems: blood levels of uric acid; blood levels of asymmetric dimethylarginine (ADMA), a blocker of NO production; and urine levels of endothelin-1.
- Sitaxentan treatment led to statistically significant reductions in all three of these markers.
- Sitaxentan reduced proteinuria (an excess excretion of protein in the urine) to a significantly greater extent than nifedipine. Proteinuria is an indicator of kidney dysfunction.
- Nifedpine and sitaxentan both reduced blood pressure to a similar extent.

"The current study shows, for the first time, that ETA receptor antagonism selectively lowers novel cardiovascular risk factors in patients with kidney disease independent of blood pressure. These effects were seen in patients already receiving optimal treatment," said Dr. Dhaun. "These findings suggest a potential role for ETA receptor antagonism in conferring additional longer-term cardiovascular and renal benefits in patients with kidney disease," he added.

More information: The article, entitled "Endothelin-A Receptor Antagonism Modifies Cardiovascular Risk Factors in CKD," will appear online: doi: 10.1681/2012040355

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