Diabetes drug shows potential for treating one cause of chronic kidney disease

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The antidiabetes drug rosiglitazone may have the potential to protect kidney function in patients with a condition called focal segmental glomerulosclerosis (FSGS), according to a study appearing in the January 2009 issue of the *Clinical Journal of the American Society Nephrology (CJASN)*. The phase I clinical findings indicate that the drug warrants further study in phase II and phase III trials.

Patients with FSGS—a condition that affects kidney function by attacking the glomeruli units within the kidney that filter blood—have limited treatment options. These individuals develop scarred or hardened blood vessels within the kidney, making the organ inefficient at filtering wastes from the blood. This condition can lead to abnormal levels of various proteins circulating through the body. Many of these patients go on to develop chronic kidney disease and will need to undergo dialysis or kidney transplantation.

In animal studies, the antidiabetes drug rosiglitazone and other medications in its class have exhibited positive effects on the kidney. To investigate the potential of rosiglitazone for treating patients with FSGS, Howard Trachtman, MD, at the Schneider Children's Hospital in New Hyde Park, New York and his colleagues designed a phase I clinical trial in patients with this condition. The study is being done in conjunction with Debbie Gipson, MD, MSPH, at the University of North Carolina in Chapel Hill, North Carolina. It is part of a comprehensive strategy to develop antifibrotic therapies for FSGS.

The investigators studied 11 patients with FSGS whose condition had not responded to previous treatment with steroids and other immunosuppressive drugs. Patients ranged from ages 2 to 28 years. Because a phase I trial is a preliminary study done before an agent's effectiveness is measured, the researchers focused on determining the safety and appropriate dosing of rosiglitazone in patients enrolled in the study.

Patients receiving rosiglitazone at a dose of three mg/m2 per day for 16 weeks experienced no serious adverse effects, including no cardiovascular complications that have been associated with rosiglitazone in other studies.

The investigators also evaluated patients' total exposure over time to rosiglitazone—in other words, how much and how long the drug stays in the body. They assessed whether certain clinical parameters such as urinary protein excretion, blood levels of the protein albumin, and kidney filtration rate might affect the drug's activity. They also looked to see if demographic factors including age, pubertal status, and body surface area had any effects. Serum albumin and kidney filtration had significant effects on the body's exposure to rosiglitazone. Other clinical parameters and demographic factors did not seem to play a role.

According to the authors, the results from this study indicate that rosiglitazone warrants further investigation for the treatment of FSGS. Because a dose of three mg/m2 per day was safe and well tolerated in this trial, this dose or higher should be investigated in later-stage studies.

Source: American Society of Nephrology