Diabetes Trials Take Kidneys into Consideration

Type 1 diabetes’ risk of developing impaired glomerular filtration decreased 50 percent when they were given intensive diabetes therapy, according to late-breaking clinical trial results presented at Kidney Week. Other late-breaking findings pointed to the promising clinical potential of sitagliptin for patients with type 2 diabetes who have moderate or severe chronic renal insufficiency.

Diabetes and kidney dysfunction often go hand-in-hand, so researchers know that it’s important to study the effects of diabetes drugs on the kidneys and to examine the safety of these drugs in patients who already have kidney disease.

In the first study, the Diabetes Control and Complications Trial (DCCT), Ian de Boer, MD, of the University of Washington, and his team looked to see if intensive diabetes therapy aimed at reducing blood sugar as close to the normal range as possible might protect type 1 diabetes’ kidney function.

“Persons with type 1 diabetes are at high risk of developing kidney disease, but no interventions are proven to prevent the development of impaired glomerular filtration rate, or GFR, in this population,” de Boer said.

The researchers randomly assigned 1441 individuals with type 1 diabetes to intensive diabetes therapy or to conventional diabetes therapy, aimed at preventing symptoms of high blood sugar. Patients were treated for an average of 6.5 years. Subsequently, 1375 participants were followed in the observational Epidemiology of Diabetes Interventions and Complications Study (EDIC).

Over an average of 22 years in DCCT/EDIC, intensive therapy was more effective at preserving long-term kidney function in study participants. A total of 24 participants assigned to intensive therapy and 46 assigned to conventional therapy developed impaired GFR, meaning that intensive diabetes therapy reduced patients’ risk by 50 percent. Of those with impaired kidney function, 8 assigned to intensive therapy and 16 assigned to conventional therapy developed kidney failure.

Compared with conventional therapy, intensive therapy reduced mean estimated GFR by 1.7 mL/min/1.73 m² during the DCCT but slowed the rate of GFR loss and increased the mean estimated GFR by 2.5 mL/min/1.73 m² during EDIC. So small short-term reductions in GFR within the normal range were followed by long-term GFR preservation. The beneficial effect of intensive therapy on impaired GFR was fully explained by lower hemoglobin A1c and lower albumin excretion rate.

“This important study shows that loss of kidney function is potentially preventable in people with type 1 diabetes and adds to our understanding of the importance of controlling blood sugar in this population,” said Marcello Tonelli MD, who moderated the late-breaking oral abstract session. Tonelli is president of the Canadian Society of Nephrology and a founding member of the Alberta Kidney Disease Network.

Another study compared the efficacy and safety of blood-sugar-lowering drugs in patients with type 2 diabetes and chronic renal insufficiency (CRI). Previous research indicates that two of these drugs, sitagliptin and glipizide, may not cause considerable kidney damage. The agents act on different targets but generate the same result—they boost the effects of insulin, which lowers blood sugar levels.

Juan Arjona Ferreira, MD, of MSD Corp. and his colleagues conducted a 54-week study to compare the efficacy and safety of sitagliptin and glipizide in patients with type 2 diabetes and moderate or severe CRI who were not on dialysis. The researchers randomized 426 patients to receive sitagliptin or glipizide. The sitagliptin dose was 50 mg once daily for patients with moderate CRI and 25 mg once daily for patients with severe CRI. The dose was adjusted downward (from 50 to 25 mg once daily) for patients whose renal status changed from moderate to severe based on confirmed estimated GFR values. The glipizide dose was 2.5 mg once daily and could be titrated up to 10 mg twice daily. The primary efficacy endpoint was the mean change from baseline in A1c. The primary safety endpoint was the incidence of adverse events of symptomatic hypoglycemia, or dangerously low blood sugar levels.

At the end of the study, blood glucose levels dropped to a similar extent in patients in both groups. Patients receiving sitagliptin were less likely to experience hypoglycemia than patients receiving glipizide (6.2 percent vs. 17.0 percent). Also, patients who took sitagliptin tended to lose a small amount of weight, while most patients who took glipizide experienced a slight weight gain.