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Early, intensive therapy for type 1 diabetes prevented kidney disease in long-term study

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Maintaining good glucose control early in the course of type 1 diabetes could lessen the long-term risk of kidney disease, as measured by a common test of kidney function.

This finding comes from more than two decades of research on preventing life-shortening complications of type 1 diabetes. The National Institutes of Health (NIH) funded the longitudinal study. Results will be published online Nov. 12 in the *New England Journal of Medicine* and presented Nov. 12 at the American Society of Nephrology Kidney Week in Philadelphia.

Researchers at the University of Washington (UW) in Seattle and several collaborating institutions in the United States and Canada examined the effects of early, intensive glucose-lowering therapy on glomerular filtration rates (GFR). This measurement estimates how much blood passes each minute through tiny filters in the kidneys. A GFR blood test checks the kidney's ability to rid the body of a muscle-generated waste product, creatinine. If the kidneys can't filter fast enough, the substance builds up in the blood.

A low GFR is a dangerous sign of existing diabetic kidney disease that can progress to kidney failure, also called end-stage kidney disease, which requires dialysis or kidney transplantation. Moreover, a low GFR also can contribute to the heart and blood vessel complications of diabetes, the researchers explained.

People with type 1 diabetes are prone to kidney disease and related complications resulting in disability and premature death. Until this study, no interventions for this population have been shown to prevent impaired GFR.

According to Dr. Ian de Boer, UW assistant professor of medicine, Division of Nephrology, once GFR is impaired, progression to end-stage kidney disease and major blood vessel disease precipitating heart attacks or stroke "occurs at unacceptably high rates, even with optimal medical management."

"This underscores the need to find ways to prevent impaired glomerular filtration rates among persons with type 1 diabetes," said de Boer.

de Boer is a UW Medicine kidney specialist at the Kidney Research Institute. He led the group that researched the effects of intensive diabetes therapy, compared to traditional diabetes treatment, on the development of impaired GFR.

The project draws on continuous studies over 28 years of 1,441 participants with type 1 diabetes mellitus. These patients originally enrolled between 1983 to 1989 in the Diabetes Control and Complications Trial (DCCT). At the time, the participants were between 13 and 39 years of age. The enrollees either showed no small blood vessel complications of their diabetes, or had only mild signs.

de Boer explained, "The DCCT was a multicenter clinical trial in diabetes mellitus that examined the effects of intensive therapy aimed at lowering blood sugar levels as close to the normal range as safely possible."

Participants randomly assigned to intensive therapy had three or more insulin injections a day, or used an insulin pump. Those in conventional

therapy had the goal of preventing symptoms of low blood sugar and high blood sugar with one or two daily insulin injections.

On average, participants in the intensive diabetes therapy group achieved a hemoglobin A1c of 7.3 percent, compared with 9.1 percent for participants in the conventional therapy group. Hemoglobin A1c is a quarterly blood sugar level test that indicates how well diabetes is being controlled.

When the DCCT ended in 1993, all participants were encouraged to join a follow-up, the Epidemiology of Diabetes Interventions and Complications Study (EDIC). Conventional therapy patients were taught intensive therapy, and those on intensive therapy were encouraged to continue intensive treatment. All returned to their own physicians for diabetes care.

By 2009, the mean age of the participants was 50 years and their mean duration of diabetes was 28 years. At that point the blood level of creatinine was measured in 85 percent of all participants (1, 222 people).

Examining results collected each year from 1983 through 2009, the researchers found that 70 participants developed impaired GFR: 24 from the initial intensive therapy group, and 46 from the group that had started out on conventional therapy.

This represented a reduced risk of developing impaired GFR by 50 percent over a total median participant follow-up of 22 years, they reported.

"This effect was only evident more than 10 years after the patients were randomized in the initial Diabetes Control and Complications Trial, beyond the period of the trial's intervention," the researchers noted.

In the present study, end-stage kidney disease developed in 8 participants in the intensive diabetes therapy group and 16 in the conventional therapy group. This represented a 51 percent reduction in risk that was not statistically significant, possibly due to the small numbers of participants reaching kidney failure.

The researchers added that the study results reported today reinforce findings of other studies on the importance of early, intensive control of blood sugar levels in type 1 diabetes. Previous research has shown benefits in reducing retina damage, nerve damage and cardiovascular disease.

The researchers stressed that this study did not look at people with type 2 diabetes, and cautioned that risks and benefits may differ in type 2 diabetes or among individuals with more advanced diabetes complications.

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