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STUDY QUESTIONS CERTAIN TREATMENTS FOR DIABETIC PATIENTS AT HIGH RISK FOR HEART DISEASE

Highlight

- In patients with type 2 diabetes at high risk for cardiovascular disease, targeting blood sugar to normal levels (HbA1c<6.0%) reduced the risk for macroalbuminuria (a high amount of protein excreted in the urine) over an average follow-up of 7.7 years, but it had no impact on more significant kidney outcomes such as serum creatinine doubling (a marker of worsening kidney function) or the need for dialysis or transplantation.
- Targeting low blood pressures (<120mmHg) or the use of fenofibrate to lower cholesterol increased the risk for doubling of serum creatinine, although it had no impact on the need for dialysis or transplantation.

Washington, DC (October 25, 2018) — New research suggests that attempts to normalize blood pressure, and cholesterol may have negative long-term effects on kidney health in adults with type 2 diabetes who are at high risk for cardiovascular disease. The results appear in an upcoming issue of the *Clinical Journal of the American Society of Nephrology (CJASN)* and will be presented at ASN Kidney Week 2018.

Type 2 diabetes greatly increases the risk for both cardiovascular disease and chronic kidney disease. Therefore, it is especially important to protect the heart and kidney health of patients with type 2 diabetes. In these patients, aggressive control of blood sugar, blood pressure, and cholesterol has resulted in conflicting short-term effects on kidney health. To determine the long-term kidney effects of these interventions, Amy K. Mottl, MD (University of North Carolina Kidney Center), Timothy E. Craven, MSPH (Wake Forest School of Medicine), and their colleagues examined information on more than 10,000 participants in ACCORDION, which is an extension phase of the ACCORD trial, a multifactorial intervention study in people with type 2 diabetes at high risk for cardiovascular disease.

The team found that intensive blood sugar control aiming for normal average blood sugar (hemoglobin A1c target <6%) reduced the risk for macroalbuminuria (a high amount of protein excreted in the urine) over an average follow-up of 7.7 years, but it had no impact on more significant kidney outcomes such as serum creatinine doubling (a marker of

worsening kidney function) or the need for dialysis or transplantation. Intensive control of blood pressure or the use of fenofibrate to lower cholesterol increased the risk for doubling of serum creatinine but did not increase the need for dialysis or transplantation.

“These results, along with those from the primary study which showed no benefit of the interventions on heart attacks and strokes, provide evidence *against* aggressive targets for glucose, blood pressure, and use of fenofibrate in adults with type 2 diabetes at high risk of cardiovascular events,” said Dr. Mottl.

An accompanying editorial takes issue with some of the conclusions. “In our view, the findings observed for doubling of serum creatinine do not suggest harm to the kidneys, but rather are more likely to reflect the limitations of the small number of creatinine measurements available,” the authors wrote. “We believe that the data actually suggest possible benefit for ESKD [end-stage kidney disease] with intensive glucose control, and remain inconclusive for intensive blood pressure control and fibrate use given the wide confidence intervals for the more reliable ESKD outcomes.”

Study co-authors include John B. Buse, MD, PhD, Faramarz Ismail-Beigi, MD, Ronald J. Sigal, MD, MPH, Carolyn F. Pedley, MD, Vasilios Papademetriou, MD, Dsc, Debra L. Simmons, MD, MS, Lois Katz, MD, and Josyf C. Mychaleckyj, DPhil.

Disclosures: J.B.B. has received contracted consulting fees, paid to his institution, and travel support from Adocia, AstraZeneca, Dexcom, Elcelyx Therapeutics, Eli Lilly, Intarcia Therapeutics, Lexicon, Metavention, NovaTarg, Novo Nordisk, Sanofi, Senseonics, and vTv Therapeutics; and grant support from AstraZeneca, Boehringer Ingelheim, Johnson & Johnson, Lexicon, Novo Nordisk, Sanofi, Theracos, and vTv Therapeutics. He holds stock options in Mellitus Health and PhaseBio and served on the board of the AstraZeneca HealthCare Foundation. He is supported by a grant from the National Institutes of Health (UL1TR002489). F.I.-B. is a consultant for NovoNordisk, Covance, Bayer, and Sanofi and holds grants from Novo Nordisk and the National Institutes of Health. J.C.M. received a research grant from Abbott Laboratories to study kidney function in the ACCORD lipid trial. A.K.M., R.J.S., C.F.P., V.P., D.L. S., L.K., and T.E.C. have no relevant disclosures.

The article, entitled “Long-Term Effects of Intensive Glycemic and Blood Pressure Control and Fenofibrate Use on Kidney Outcomes,” will appear online at <http://cjasn.asnjournals.org/> on October 25, 2018, doi: 10.2215/CJN.06200518, and will be presented at ASN Kidney Week 2018 during a session entitled, “Best of ASN Journals: CJASN and JASN” (<https://www.asn-online.org/education/kidneyweek/2018/program-session-details.aspx?sessId=288128>).

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Tweet: Aggressive treatment of blood pressure and cholesterol may result in poor kidney outcomes in some patients with type 2 diabetes.

Facebook: New research suggests that aggressive targets for blood sugar, blood pressure, and cholesterol may have negative long-term effects on kidney health in adults with type 2 diabetes who are at high risk for cardiovascular disease. The results appear in the *Clinical Journal of the American Society of Nephrology*.

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