Nature Reviews Nephrology **10**, 481 (2014); published online 5 August 2014; doi:10.1038/nrneph.2014.140

DIABETES

Intensive glucose-lowering: long-lasting benefits on albuminuria in patients with type 1 diabetes

Studies have shown that intensive regimens to lower blood glucose levels in patients with diabetes mellitus provide microvascular protection that lasts beyond the duration of treatment; however, the extent to which these effects persist is unknown. A new report published in *The Lancet Diabetes & Endocrinology* demonstrates that the benefits of intensive glucose-lowering treatment on development of albuminuria persist for 18 years after its application.

Kidney disease is a major and common complication of diabetes, with albuminuria often being the first sign of kidney damage. The presence of albuminuria in patients with type 1 or type 2 diabetes is associated with adverse health outcomes, and prevention of albuminuria and kidney disease is therefore an important goal in the management of these patients.

To investigate the long-term effects of intensive glucose control in patients with type 1 diabetes, Ian de Boer and colleagues performed a follow-up of the Diabetes Control and Complications Trial (DCCT) and the Epidemiology of Diabetes Interventions and Complications (EDIC) study. "We asked whether the renal benefits of intensive diabetes therapy were durable over long-term follow-up in type 1 diabetes," explains de Boer. The DCCT was a multicentre randomized clinical trial in which 1,441 patients with type 1 diabetes were randomly assigned to receive either intensive or conventional diabetes treatment. The goal of intensive treatment was to achieve levels of glycaemia as close to the nondiabetic range as safely possible, whereas the goal of conventional treatment was to prevent symptoms of hyperglycaemia and hypoglycaemia. After a mean follow-up of 6.5 years, all participants were instructed in intensive treatment and were returned to their own health-care providers for continued care. 96% of participants agreed to join the observational EDIC study for follow-up, during which the researchers measured participants' serum creatinine levels every year and albumin excretion rate every 2 years for a mean of 17.2 years. "We already knew from the DCCT that intensive therapy aimed at controlling blood glucose levels as close as possible to the normal range reduces the risk of albuminuria, and from the EDIC study that the benefits of intensive therapy persisted for at least 8 years after the DCCT ended," says de Boer. "Here, we extended follow-up for an additional 10 years, totalling 18 years after conclusion of the DCCT."

During years 1–18 of EDIC, the researchers identified 191 new cases of microalbuminuria, defined as an albumin excretion rate ≥30 mg per 24 h on two consecutive study visits. Development of microalbuminuria was more common in patients who had been assigned to receive conventional treatment during the DCCT than in those who received intensive treatment (120 versus 71 patients, respectively; risk reduction 45%, 95% CI 26–59%). Development of macroalbuminuria was also more common in patients who had received conventional therapy (86 versus 31 patients; risk reduction 61%, 95% CI 41–74%). Of note, however, the increased risk of developing albuminuria in the group assigned to receive conventional therapy during the DCCT declined over time. Compared to patients who received intensive treatment, the risk of incident microalbuminuria for patients assigned to receive conventional treatment was considerably higher during years 1–8 of EDIC than during years 9–18 of EDIC. Risk reduction for intensive versus conventional therapy during the DCCT was 58% (95% CI 40–71%; $P<0.001$) during EDIC years 1–8 versus 10% (95% CI −46–44%; $P=0.68$) during EDIC years 9–16. The researchers noted

Sunstock/iStock/Thinkstock

a similar pattern for macroalbuminuria. At year 17–18 of EDIC, however, the prevalence of albuminuria was higher in patients assigned to receive conventional treatment during the DCCT than in those who received intensive therapy (24.9% versus 18.4%, respectively; $P=0.02$).

Over the combined course of the DCCT and EDIC, the researchers identified more cases of incident impaired glomerular filtration rate (GFR), defined as an estimated GFR <60 ml/min/1.73 m^2 on two consecutive study visits, in patients who received conventional diabetes treatment during the DCCT than in those who received intensive treatment (53 versus 31 patients, respectively; risk reduction 44%, 95% CI 12–64%). Most of these events occurred during the EDIC study. "These findings reinforce the long-term renal benefits of tight glucose control in type 1 diabetes and emphasize the importance of early intensive diabetes therapy in this population," explains de Boer.

Susan J. Allison

Original article de Boer, I. H. *et al*. Effect of intensive diabetes treatment on albuminuria in type 1 diabetes: long-term follow-up of the Diabetes Control and Complications Trial and Epidemiology of Diabetes Interventions and Complications study. *Lancet Diabetes Endocrinol*. doi:10.1016/S2213-8587(14)70155-X