COMMENTS AND RESPONSES

Response to Comment on: Chakkera et al. Can New-Onset Diabetes After Kidney Transplant Be Prevented? Diabetes Care 2013;36:1406–1412

Hecking et al. raise several important questions in their letter (1). First, compared with classic type 2 diabetes, how important is insulin sensitivity in the development of new-onset diabetes after transplantation (NODAT)? Second, compared with type 1 or type 2 diabetes, is NODAT more rapid in onset? Finally, what are the relative contributions of lifestyle intervention and exogenous insulin in prevention or early therapy of NODAT?

Abnormalities in both insulin sensitivity and insulin secretion are central to the development of type 2 diabetes and NODAT. We hypothesized in our article that both increase in insulin resistance and impairment in insulin secretion can tip patients toward development of NODAT, similar to the roles of these abnormalities in producing type 2 diabetes in people not undergoing transplantation (2). The contributions of insulin sensitivity and secretion in the development of type 2 diabetes were investigated in the Diabetes Prevention Program (3). In this large clinical trial of people at high risk of type 2 diabetes, both impaired insulin sensitivity and impaired insulin secretion predicted development of type 2 diabetes. The lifestyle and metformin interventions led to improvements in estimated insulin sensitivity, concomitant improvement in secretion relative to sensitivity, and reduction in the incidence of diabetes. Similarly, we hypothesize that behavioral interventions including regular physical activity and weight control in patients undergoing kidney transplantation may reduce the risk of NODAT.

Unlike classic type 1 or type 2 diabetes, NODAT may be precipitated by surgical stress, immunosuppressant drugs, and postoperative weight gain during the first year after transplantation. Nevertheless, NODAT shares many risk factors with type 2 diabetes, suggesting common features in its pathogenesis. This is the basis for our hypothesis that preventive measures known to reduce the incidence of type 2 diabetes in nontransplant settings may similarly reduce the incidence of NODAT or of transient postoperative hyperglycemia. Our hypothesis requires testing in randomized clinical trials.

Basal exogenous insulin therapy reduced the incidence of new-onset type 2 diabetes in patients with cardiovascular risk factors plus impaired fasting glucose or impaired glucose tolerance (4), but, to our knowledge, exogenous insulin is rarely used for type 2 diabetes prevention. Exogenous insulin does not prevent type 1 diabetes in patients at high risk (5). We agree with Hecking et al. that exogenous insulin is an appropriate treatment for hyperglycemia in the immediate postoperative period. Impaired insulin secretion may be important in the development of NODAT during that time. Behavioral interventions and exogenous insulin administration are not mutually exclusive, and both may play important roles in preventing NODAT. Given the high incidence and serious consequences of NODAT, all preventive measures should be identified and evaluated.

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References

1. Hecking M, Sharif A, Port FK, Säemann MD. Comment on: Chakkera et al. Can new-onset diabetes after kidney transplant be prevented? Diabetes Care 2013;36:1406–1412 (Letter). Diabetes Care 2013;36:e182. DOI: 10.2337/dc13-1277
2. Chakkera HA, Weil EJ, Pham PT, Pomeroy J, Knowler WC. Can new-onset diabetes after kidney transplant be prevented? Diabetes Care 2013;36:1406–1412
3. Kitabchi AE, Temprosa M, Knowler WC, et al.; Diabetes Prevention Program Research Group. Role of insulin secretion and sensitivity in the evolution of type 2 diabetes in the diabetes prevention program: effects of lifestyle intervention and metformin. Diabetes 2005;54:2404–2414
4. Gerstein HC, Bosch J, Dagenais GR, et al.; ORIGIN Trial Investigators. Basal insulin and cardiovascular and other outcomes in dysglycemia. N Engl J Med 2012;367:319–328
5. Diabetes Prevention Trial–Type 1 Diabetes Study Group. Effects of insulin in relatives of patients with type 1 diabetes mellitus. N Engl J Med 2002;346:1685–1691