COMMENT ON CUNDY ET AL.

Early Worsening of Diabetic Nephropathy in Type 2 Diabetes After Rapid Improvement in Chronic Severe Hyperglycemia. Diabetes Care 2021;44:e55–e56

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We were interested in the recent article by Cundy et al. (1), who described a rapid and durable decline of estimated glomerular filtration rate (eGFR) in four subjects with type 2 diabetes after their HbA_{1c} had fallen from 118 mmol/mol (12.9%) to 48 mmol/mol (5.5%). Fifteen years ago, we reported that GFR and its estimations correlated with HbA_{1c}, each +1% (+9 mmol/mol) HbA_{1c} being associated with +5–6 mL/min/1.73 m^2 GFR (2). One could then fear a –35 mL/min/1.73 m^2 GFR reduction after a rapid –7% reduction of HbA_{1c}.

We have recently shown that a dramatic reduction of HbA_{1c}, by more than 27 mmol/mol (–3%), could be detected during the years preceding admission in 13.5% of 680 patients hospitalized for type 2 diabetes in our ward. Proliferative diabetic retinopathies were more frequent among these "rapid HbA_{1c} decliners" (3). Cundy et al. mentioned the development of cotton wool spots on serial retinal photographs in their subjects, which prompted us to check whether diabetic kidney disease (DKD) could be related to the previous rapid decline of HbA_{1c} in our patients.

Two-hundred ninety-six of our 680 patients had DKD (43.5%). As expected, they were older (mean ± SD age 63 ± 10 years vs. 61 ± 9, $P = 0.025$), more were men (63.2% vs. 52.0%, $P = 0.004$), with a longer duration of diabetes (15 ± 10 years vs. 13 ± 9, $P = 0.001$), more arterial hypertension (71.2% vs. 63.7%, $P = 0.048$), more dyslipidemia requiring a statin (73.2% vs. 62.9%, $P = 0.005$), and more diabetic retinopathies or macular edema (37.2% vs. 22.6%, $P < 0.001$). Their HbA_{1c} at admission was, however, similar to patients without DKD at 77 ± 15 mmol/mol (8.6 ± 1.7%), and the rates of previous dramatic reductions of HbA_{1c} did not differ: 13.9% vs. 13.1% ($P = 0.938$). By binary logistic regression analysis, the previous rapid decline of HbA_{1c} was not related to DKD after adjustment for age, sex, diabetes duration, arterial hypertension, and dyslipidemia: odds ratio 1.012 (95% CI 0.796–1.285). At their admission, the eGFR of rapid HbA_{1c} decliners (85 ± 26 mL/min/1.73 m^2) did not differ compared with others (83 ± 25 mL/min/1.73 m^2, P = NS), nor did their albumin excretion rates: 17 mg/24 h (interquartile range 4–57) vs. 14 mg/24 h (4–60).

Because we did not register the renal parameters of our patients before their reduction of HbA_{1c}, we cannot exclude that some of our rapid HbA_{1c} decliners had a reduction of GFR before their admission, as observed by Cundy et al. But this did not result in more altered renal parameters at admission. Gibbons and Freeman (4) also did not mention a decline of renal function among their 16 cases of painful neuropathy after intensive glucose control, although their rates of microalbuminuria increased. In the Trial to Evaluate Cardiovascular and Other Long-term Outcomes With Semaglutide in Subjects With Type 2 Diabetes (SUSTAIN-6), higher rates of retinopathy complications were registered in the semaglutide-treated arm, probably favored by the reduction of HbA_{1c}, but there were fewer new or worsening nephropathies (5).

A dramatic worsening of renal function following the normalization of a very high HbA_{1c}, as observed by Cundy et al. (1), seems therefore exceptional. Such observations are important, however, and renal insufficiency adds to the list of deleterious consequences of rushed glucose control: hypoglycemias, worsened retinopathy (2,5), and painful neuropathy (4).

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