COMMENT ON ROSENSTOCK ET AL.

Impact of a Weekly Glucagon-Like Peptide 1 Receptor Agonist, Albiglutide, on Glycemic Control and on Reducing Prandial Insulin Use in Type 2 Diabetes Inadequately Controlled on Multiple Insulin Therapy: A Randomized Trial. Diabetes Care 2020;43:2509–2518

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We read with interest the study by Rosenstock et al. (1), which demonstrates that in patients with type 2 diabetes managed on a basal-bolus insulin regimen, switching three prandial insulin injections for a long-acting glucagon-like peptide 1 receptor agonist (GLP-1RA), albiglutide, while maintaining the basal insulin, represents an effective strategy for optimizing glycemic control with reduced risks of hypoglycemia and weight gain along with increased convenience. In the cohort studied, baseline glycated hemoglobin levels were 7.8 ± 0.6% (albiglutide group) and 7.7 ± 0.6% (placebo group), indicating that in many participants, postprandial glycemic excursions were the dominant contributor of hyperglycemia. Achieving good glycemic control in those patients would, therefore, probably require specific interventions to minimize the glycemic response to meals. The rate of gastric emptying, which exhibits a wide interindividual variation in health and may be delayed, accelerated, or normal in type 2 diabetes, has a major effect on the increase in postprandial blood glucose; when gastric emptying is relatively faster, the rise in blood glucose is greater (2). The excellent commentary that accompanies this article appropriately alludes to the effects of GLP-1RAs on gastric emptying (3). We agree that short-acting GLP-1RAs, such as exenatide twice a day and lixisenatide, have a sustained effect of slowing gastric emptying substantially (2), but recent studies using the gold standard technique of scintigraphy have established that the long-acting GLP-1RAs exenatide once a week (4) and liraglutide (5) also slow gastric emptying significantly after steady-state administration, contrary to previous thought. While the effects of long-acting GLP-1RAs on slowing gastric emptying are almost certainly less than those of short-acting GLP-1RAs, reflecting their different pharmacokinetic properties with more sustained GLP-1 receptor activation, they are still substantial. Moreover, the magnitude of the postprandial glucose lowering relates to the extent of slowing gastric emptying and is greater when baseline gastric emptying is relatively more rapid in a given individual (2). Accordingly, measurement of gastric emptying by scintigraphy or, often more readily, with a stable isotope breath test, in addition to the baseline glycated hemoglobin, has the potential to determine the choice of GLP-1RA in patients with type 2 diabetes managed with basal insulin. Those in whom gastric emptying is relatively more rapid, and with an HbA_{1c} <8%, would intuitively be expected to benefit from a short-acting GLP-1RA that slows gastric emptying markedly; this hypothesis should be addressed in clinical trials.

Duality of Interest. C.S.M. has participated in symposia or educational sessions for Novo Nordisk, Eli Lilly, Merck Sharp & Dohme, Boehringer Ingelheim, and AstraZeneca and has received honoraria for this activity. K.L.J. has received research funding from Sanofi and AstraZeneca and study medication from Merck Sharp & Dohme. C.K.R. has received research funding from AstraZeneca, Merck Sharp & Dohme, Eli Lilly, Novartis, and Sanofi. T.W. has received research funding from Novartis and AstraZeneca. M.H. has participated in advisory boards and/or symposia for Novo Nordisk, Sanofi, Novartis, Eli Lilly, Merck Sharp & Dohme, Boehringer Ingelheim, and AstraZeneca and has received honoraria for this activity. No other potential conflicts of interest relevant to this article were reported.

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