COMMENTS AND RESPONSES

Comment on: Luijf et al. Premeal Injection of Rapid-Acting Insulin Reduces Postprandial Glycemic Excursions in Type 1 Diabetes. Diabetes Care 2010;33: 2152–2155

Referring to the article by Luijf et al. (1), administrating rapid-acting insulin analogs 15 min before mealtimes resulted in fewer episodes of postprandial hyperglycemia and more time spent in the 3.5–10.0 mmol/L range, without increased risk of hypoglycemia. No effect was noted when administered 30 min before meals. Authors speculate that if insulin administered 15 min before the meal is optimum, then both −30 and 0 min treatment periods had an equal 15 min mismatch, resulting in almost equal postprandial glycemic control.

In our opinion (2), it is a matter of mimicking the "cephalic phase," which is lost in patients with type 1 diabetes. A recent study (3) shows the mechanisms and physiological relevance of the cephalic insulin response to meal ingestion in healthy subjects, attributed to autonomic activation mediated by noncholinergic and cholinergic mechanisms, lasts for about 10 min, is initiated by meal ingestion, and is required for normal postprandial glucose tolerance (3).

In subjects with type 1 diabetes, who have lost the endogenous insulin secretion, it might be hypothesized that by preceding a meal by an insulin bolus injected 15 min before could replace this "cephalic phase," provided that the glycemia before the meal is in the normal (1,2) range. If the preprandial glycemia is above the normal range, 15 min would not be enough time to anticipate a normal postprandial response. We observed in 69 children and adolescents (37 male and 32 female) aged 4–21 years (mean ± SD 14.9 ± 4.4 years), with type 1 diabetes for 8.4 ± 4.5 years (BMI 21.8 ± 4.1 m/kg^2, insulin requirement 0.80 ± 0.24 units/kg/day, HbA_{1c} 8.1 ± 1.3%) undergoing TYpe of BOlus in children with DIabetes (TyBoDi) studies (A.E.S., unpublished data) that when the preprandial glycemia is above 10.0 mmol/L, injecting the bolus 15 min prior to a meal is not sufficient enough to prevent 60-, 90-, 120-min postprandial hyperglycemia (11.2 ± 1.9, 11.9 ± 2.1, and 11.6 ± 1.7 mmol/L, respectively), irrespective of the type of bolus used. In this case, it is better to inject the bolus 30–60 min prior to a meal. However, in our experience, to separate the correction bolus from the meal bolus has the following results: −30 min experiment: premeal 11.2 ± 1.9, 60 min 11.8 ± 1.7, 90 min 11.5 ± 1.7, and 120 min 10.8 ± 2.2 mmol/L; −60 min experiment: premeal 11.3 ± 1.9, 60 min 10.8 ± 3.1, 90 min 10.5 ± 2.7, 120 min 10.3 ± 2.7 mmol/L; separate bolus experiment (correction given −45 and meal bolus given −15 min prior meal): premeal 11.2 ± 2.3, 60 min 8.7 ± 2.7, 90 min 7.3 ± 3.2, 120 min 7.9 ± 3.6 mmol/L; $P = 0.002$ by ANOVA.

The observations reported by Luijf et al. (1) and our group (2,4) demonstrate that with new technology such as the insulin pump and with new rapid-acting insulin analogs, amount and timing of bolus are both important for people with diabetes to reach the goals of the American Diabetes Association, the European Association for the Study of Diabetes, and the International Society for Pediatric and Adolescent Diabetes. Looking in depth into the daily habits of our patients may shed light onto how we can improve their glycemic control and, most of all, quality of life. Further studies are needed to evaluate the impact of different types of bolus (simple vs. double-wave) for different types of meals with different absorption times on glycemia.

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