# Food Order Has a Significant Impact on Postprandial Glucose and Insulin Levels

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*Diabetes Care 2015;38:e98–e99 | DOI: 10.2337/dc15-0429*

Postprandial hyperglycemia is an important therapeutic target for optimizing glycemic control and for mitigating the proatherogenic vascular environment characteristic of type 2 diabetes. Existing evidence indicates that the quantity and type of carbohydrate consumed influence blood glucose levels and that the total amount of carbohydrate consumed is the primary predictor of glycemic response (1). Previous studies have shown that premeal ingestion of whey protein, as well as altering the macronutrient composition of a meal, reduces postmeal glucose levels (2–4). There are limited data, however, regarding the effect of food order on postprandial glycemia in patients with type 2 diabetes (5). In this pilot study, we sought to examine the effect of food order, using a typical Western meal, incorporating vegetables, protein, and carbohydrate, on postprandial glucose and insulin excursions in overweight/obese adults with type 2 diabetes.

A total of 11 subjects (6 female, 5 male) with metformin-treated type 2 diabetes were studied using a within-subject crossover design. The average (mean ± SD) age and BMI were 54 ± 9 years and 32.9 ± 5 kg/m$^2$, respectively. The average duration of diabetes was 4.8 ± 2.4 years and the mean $HbA_{1c}$ was 6.5 ± 0.7%.

After a 12-h overnight fast, subjects consumed an isocaloric meal (628 kcal: 55 g protein, 68 g carbohydrate, and 16 g fat) with the same composition on 2 separate days, 1 week apart. During the first visit, the food order was carbohydrate (ciabatta bread and orange juice), followed 15 min later by protein (skinless grilled chicken breast) and vegetables (lettuce and tomato salad with low-fat Italian vinaigrette and steamed broccoli with butter); the food order was reversed a week later. Blood was sampled for glucose and insulin measurements at baseline (just before meal ingestion) and 30, 60, and 120 min after the start of the meal.

The mean postmeal glucose levels were decreased by 28.6% ($P = 0.001$), 36.7% ($P = 0.001$), and 16.8% ($P = 0.03$) at 30, 60, and 120 min, respectively, and the incremental area under the curve ($iAUC_{0–120}$) was 73% lower (2,001 ± 376.9 vs. 7,545 ± 804.4 mg/dL × 120 min, $P = 0.001$) when vegetables and protein were consumed first, before carbohydrate, compared with the reverse food order (Table 1). Postprandial insulin levels at 60 and 120 min and the $iAUC_{0–120}$ were also significantly lower when protein and vegetables were consumed first.

In this pilot study, we demonstrated that the temporal sequence of carbohydrate ingestion during a meal has a significant impact on postprandial glucose and insulin excursions. The magnitude of the effect of food order on glucose levels is comparable to that observed with pharmacological agents that preferentially target postprandial glucose. Moreover, the reduced insulin excursions observed in this experimental setting suggest that this meal pattern may improve insulin sensitivity. A limitation of the study is that we analyzed glucose and insulin responses up to 120 min following meal ingestion, as this study was designed to test postprandial glucose levels as practically measured by patients with type 2 diabetes. Further studies with longer follow-up to delineate the full impact, including delayed effects and the mechanisms underlying the glycemic effect of food order, are indicated.

In contrast to conventional nutritional counseling in diabetes, which is largely restrictive and focuses on "how much" and "what not to eat," this pilot study suggests that improvement in glycemia may be achieved by optimal timing of carbohydrate ingestion during a meal.

**Acknowledgments.** The authors thank David Ludwig, MD, PhD (Boston Children's Hospital, Boston, MA), for helping formulate the study hypothesis.

**Funding.** This study was supported by the Clinical and Translational Science Center at Weill Cornell Medical College (UL1 TR000457) and the Dr. Robert C. and Veronica Atkins Curriculum in Metabolic Disease at Weill Cornell Medical College Grant.

**Duality of Interest.** No potential conflicts of interest relevant to this article were reported.

**Author Contributions.** A.P.S. designed the study, conducted study procedures, analyzed and interpreted data, and wrote the manuscript. R.G.I. researched data, conducted study procedures, analyzed data, and edited the manuscript. C.E.T. conducted study procedures and edited the manuscript. L.J.A. designed the study, interpreted data, and reviewed and edited the manuscript. A.P.S. and L.J.A. are the guarantors of this work and,

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**Table 1—Glucose and insulin levels/iAUC for various time points/intervals during the two visits**

| | Time (min) | Carbohydrates first | Carbohydrates last | $P^c$ | Change (%) |
|---|---|---|---|---|---|
| Blood glucose (mg/dL)[a] | 0 | 106.7 ± 5.3 | 107.3 ± 6.3 | 0.752 | 0.5 |
| | 30 | 156.8 ± 8.2 | 112.0 ± 5.8 | 0.001 | −28.6 |
| | 60 | 199.4 ± 12.2 | 125.6 ± 6.9 | 0.001 | −37.0 |
| | 120 | 169.2 ± 13.8 | 140.8 ± 7.7 | 0.030 | −16.8 |
| Serum insulin (μIU/mL)[a] | 0 | 18.8 ± 2.4 | 16.3 ± 1.4 | 0.154 | −13.6 |
| | 30 | 62.4 ± 8.6 | 42.9 ± 9.7 | 0.083 | −31.2 |
| | 60 | 125.4 ± 20.1 | 63.2 ± 11.0 | 0.002 | −49.6 |
| | 120 | 152.0 ± 31.7 | 90.9 ± 16.6 | 0.014 | −40.2 |
| Glucose iAUC (mg/dL × min)[b] | 0–30 | 751.4 ± 71.0 | 90.0 ± 26.8 | 0.001 | −88.0 |
| | 0–60 | 3,396.8 ± 606.9 | 444.2 ± 103.8 | 0.001 | −86.9 |
| | 0–120 | 7,545.0 ± 804.4 | 2,001.5 ± 376.9 | 0.001 | −73.5 |
| Insulin iAUC (μIU/mL × min)[b] | 0–30 | 657.5 ± 131.8 | 399.5 ± 132.6 | 0.102 | −39.2 |
| | 0–60 | 2,908.5 ± 432.0 | 1,510.5 ± 407.4 | 0.002 | −48.1 |
| | 0–120 | 10,097.9 ± 1,646.9 | 5,202.8 ± 1,061.6 | 0.002 | −48.5 |

Data are means ± SEM, $n = 11$. [a]Blood samples were collected immediately before the meal ($t = 0$ min) and at 30, 60, and 120 min after the start of the meal. [b]Intervals were measured in minutes from the start of the meal. [c]*P* values were calculated using the Wilcoxon matched-pairs signed rank test.

as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Prior Presentation.** The glucose data were presented as a late-breaking abstract at the Obesity Society 2014 Annual Scientific Meeting ObesityWeek, Boston, MA, 2–7 November 2014.

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