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Predicting more accurately the overall glucose response to a lunch meal by using the postprandial glucose peak

Didier Chapelot[a,*], Corinne Marmonier[a], Paul Valensi[b]

[a]*Laboratory of Cellular and Functional Responses to Hypoxia, University Paris 13, Bobigny 93017, France*
[b]*Department of Endocrinology, Diabetes and Nutrition, Jean Verdier Hospital, Bondy, France*

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Abstract

Although the assessment of postprandial glycemia is clinically important, the most relevant time points with the smallest number of blood samples giving the highest predictive power have yet to be established. It has been suggested that a sample estimating the postprandial peak concentration would improve this predictive power compared to the usual recommended time points. In this study, we assessed the power of these time points to predict the glucose response to a meal mimicking everyday life. Subjects were 11 healthy young men (mean age, 22 ± 1 years; body mass index, 21.7 ± 1.8 kg/m^2). Plasma glucose, insulin, and nonesterified fatty acids were measured by continuous collection of blood in tubes filled every 5 minutes for 240 minutes after a 2-item lunch meal consumed ad libitum on the first test day, and in the same amount 1 week later. The most relevant time point for the plasma glucose peak level was found at 45 minutes (mean interval, 47 ± 3 minutes) and was not dependent on the energy intake at lunch. Its coefficient of variation was low (7.0% ± 1.5%). The best predictive equation for the whole postmeal glucose area under the curve (AUC) was found at 120 minutes and involved glucose, insulin, and nonesterified fatty acids (r^2 = 0.89; $P < 10^{-7}$). The 120-minute postmeal glucose profile constructed with the 0-, 45-, 90-, and 120-minute time points overlapped more accurately with the actual profile than did the time points normally used in the glucose tolerance test, and slightly improved the correlation between the calculated and the actual plasma glucose area under the curve (r = 0.96; $P < 10^{-7}$). In conclusion, in healthy, young, lean male subjects, a blood sample collected 45 minutes after a spontaneous lunch meal estimates the postprandial plasma glucose peak and suggests that including the peak level along with 90- and 120-minute time points may improve the predictive power of the plasma glucose profile after a meal.

1. Introduction

It has been suggested that a standardized, mixed test meal would be more efficient than an oral glucose tolerance test (OGTT) for assessing impaired glucose tolerance (IGT) or diabetes [1-5]. A postmeal glucose tolerance test may avoid the low acceptability of the glucose load and improve reproducibility. More recently, postprandial hyperglycemia has been considered as a possible independent cardiovascular risk factor [6-11] and among all blood glucose levels tested over the day, only blood glucose after lunch predicted cardiovascular events [12], providing strong support for this hypothesis. This led some authors [13] to conclude that "early interventional data suggest that therapy targeted at postprandial glucose can have a favorable impact on cardiovascular events." Others [14] proposed trying to restrict glucose to less than 180 or less than 140 mg/dL over postbreakfast or postlunch periods. However, the time points most predictive of the overall glucose response to the meal are unknown.

The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus [15] and the World Health Organization [16] have restricted the diagnosis of diabetes mellitus to the value of the blood glucose concentration after an 8-hour fast or to a glucose measurement 120 minutes after a 75-g glucose load dissolved in water. The other time points recommended for measuring plasma glucose to diagnose diabetes or IGT are fasting level and 30, 60 [17], or 90 minutes [18] after either a glucose load (range, 50-100 g) or a standard test meal [19].

In our 10 years' experience analyzing postmeal blood glucose profiles using continuous blood collection, we

* Corresponding author. Physiologie du Comportement Alimentaire, UFR SMBH, 74 rue Marcel Cachin, 93017 Bobigny, France. Tel.: +33 1 48 38 77 36; fax: +33 1 48 38 88 64.
E-mail address: comp-alim@smbh.univ-paris13.fr (D. Chapelot).

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found that the 120-minute time point measurement occurs during a phase of high variability. This is accounted for by the fact that in most healthy subjects, plasma glucose and insulin concentrations are biphasic after either a glucose load [20,21] or a lunch meal [22]. This variability could alter the relevance of this time point if a high glucose level corresponds to a second glucose peak profile in some but not all subjects. Moreover, the power of the different time points to predict the total glucose response to a meal has not been assessed, mainly because it needs a reference condition requiring frequent or even continuous blood collection. Last, because of the importance of a peak in pulsatile mechanisms, it seems important to test the predictive power of the time point most relevant to the postprandial glucose peak.

In the present study, blood was continuously withdrawn and collected in tubes changed every 5 minutes. We measured plasma glucose, insulin, and nonesterified fatty acid (NEFA) concentrations over 4 hours after a lunch meal, and measurements were taken twice with an interval of 1 week between the two. The time points most relevant to the peak level and the lowest coefficient of variation (CV) for predicting the overall glucose response were assessed. The best geometrical construction of the actual glucose response was tested with the time points usually recommended and with time points that we thought followed more accurately the actual blood glucose profile.

2. Materials and methods

2.1. Subjects

After approval of the protocol by the Ethics Committee in Human Research of Aulnay-sous-Bois, France, subjects were recruited through advertisements posted in the Xavier Bichat Medical School (Paris, France). Subjects were excluded if they were smokers; were trained athletes; took medication; reported a personal or family history of obesity, diabetes, or other metabolic disease; or reported a change in body weight of ±2 kg over the 3 years before the study. The experiment was completed by 11 lean and healthy men aged 22 ± 1 years (mean ± SEM). Body mass index for the group was 21.7 ± 1.8 kg/m^2. Fat-free mass and fat mass were assessed by using the subcutaneous skinfold thickness method and were estimated at 61.1 ± 6.1 and 9.0 ± 2.4 kg, respectively. Subjects gave written informed consent before the experiment and were financially compensated for completing the study.

2.2. Procedure

Subjects came to the laboratory on 2 occasions separated by an interval of 1 week. Subjects were asked to eat the same breakfast on the morning of the experimental days. This was checked with the investigator on the second session. They arrived at the laboratory at 12:15 PM. They were deprived of time cues by exposing them to artificial light and by removing all sources of visual and auditory time cues as previously described [23]. At 12:30 PM, an indwelling catheter was inserted into an antecubital vein and saline was infused for 30 minutes. Blood withdrawal started at 1:00 PM and was uninterrupted throughout the experiment. Lunch was served 30 minutes after the first blood sampling. On the first test day, subjects were told to eat as much or as little as they wanted, and meal duration was not fixed to encourage ad libitum intake. The same amount was served on the second test day, and subjects were required to eat all of it.

2.3. Test meal

Lunch meal consisted of a main dish, spaghetti "bolognaise" (5.2 kJ g^{-1}; 56% carbohydrate, 18% fat, 26% protein), and a dessert item, praline-flavored dessert cream (6.2 kJ g^{-1}; 57% carbohydrate, 30% fat, 13% protein).

2.4. Biochemical analyses

As described in detail elsewhere [23], a specially designed double-lumen catheter (MTB, Amstetten, Germany) was inserted into the antecubital vein and blood was withdrawn continuously throughout the session. Sample tubes were filled every 5 minutes and were immediately centrifuged at 4°C. Plasma was frozen to −30°C for subsequent assays. Plasma assays for glucose, insulin, and NEFA followed standard procedures. Insulin was determined by radioimmunoassay using the SB-INSI-5 kit (CEA, Gif-sur-Yvette, France; 7% accuracy) with a lower level of sensitivity of 2 μU mL^{-1}. Glucose was measured by the glucose oxidase enzymatic method in a Yellow Spring glucose analyzer (Bioblock, Strasbourg, France; 1% accuracy). NEFA concentrations were measured by the colorimetric enzymatic method using a C Wako kit (Oxoïd, Dardilly, France; 5% accuracy).

2.5. Statistical analyses

Peaks were determined, in each subject and in each test, as time points preceded and followed by at least 2 increasing and decreasing points. To select the most relevant time point for the first postprandial glucose peak, we first noted the time point where this peak occurred most often, and then we calculated the mean time interval to this peak. To be selected, the time point had to be the closest to the mean interval and the one displaying the most peaks. A glucose area under the curve (AUC) (glucose$_{AUC}$) was determined by using the trapezoidal method without subtraction of a basal AUC because the total was more important than the incremental area [24]. The CV of each time point and of glucose$_{AUC}$ was calculated for each subject according to the equation CV = 100 × SD/M, where SD is the standard deviation of the repeated tests calculated for each subject and M the mean value of the 2 tests observed for each subject. Then the mean CV was calculated for the group as the mean of all individual CVs. The lowest CV was calculated by using the same procedure