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Original

Variability of glycemic and insulin response to a standard meal, within and between healthy subjects

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Abstract

Aim: To test the variability within and between subject of glycemic response test following the ingestion of a standard food.

Material and methods: Glucose and insulin response of a standard meal (white bread) was performed in ten healthy volunteers and repeated under identical conditions for 6 times. Blood glucose and insulin levels were measured in the fasted state and over the 180 min following commencement of consumption of the foods. The Area Under the Curve (AUC) for glucose and insulin was calculated for the values above baseline for the 3-hour period following the standard meal. Within and between coefficient of variation was calculated.

Results: The total intra-individual variation of the gAUC was 51.8% range 24.9 to 91.4%. The inter-individual variation of the gAUC in the complete study was 75.2%. The total intra-individual variation of the iAUC was 51.9%. ranged: 7.7 to 103%. The inter-individual variation in the complete study was 86%.

Conclusion: Glucose and insulin response to a reference food has low reliability, therefore limits its clinical utility for individual dietary prescription.

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Key words: Glycemic. Insulin response. Variability. Standard meal.

Introduction

The glycemic index (GI) is a food classification score that depends on its potential to rise blood glucose levels after oral intake. The scientific definition corresponds to “the incremental area under the blood glucose curve (AUC) following ingestion of a test food, expressed as a percentage of the corresponding area, following an equivalent load of a reference carbohydrate, either glucose or white-wheat bread.”

Therefore, this definition alludes that the GI of a given food, depends entirely on its intrinsic characteristics, such as the type of carbohydrate, fat and protein content, acidity, physical properties, presence of viscous soluble and insoluble fibers, processing treatment of food. All these components will affect the velocity of gastric emptying, carbohydrate digestibility...
or absorption rate. In consequence, the same food given at different times, but with identical pretest standardization, should render a similar blood glucose AUC and GI in the same or different individuals. However, in the clinical practice we, as other authors, have observed that the inter-individual and intra-individual variation of the GI is very high, independent of the meal and the method of standardization.

The aim of this study was to test the variability within and between subjects of glycemic response test following the ingestion of a standard food.

Material and methods

Ten healthy volunteers of both sexes, aged between 26 and 56 years were invited to take part in the study. After subjects agreed to participate through a signed informed and written consent, they were asked to attend to the study center at the Institute of Nutrition and Food Technology, University of Chile (INTA) for a fasting blood glucose testing and recording of personal data. Exclusion criteria were pregnancy, a fasting blood glucose > 110 mg/dl, or a family history of type 1 or 2 diabetes, body mass index > 30 kg/m², being on a special diet, under medication or practicing intense physical activity for more than 90 minutes per week. Glucose and insulin response to a standard meal (white bread) was measured in each subject and repeated under identical conditions for 6 times. The first three occasions were on April-May 2009 and the last three on November-December 2009. In the 2 periods each study was performed with a minimum of 1 or a maximum of 5 weeks interval. The standard meal was white bread (110 g) obtained from a previously standardized bakery (in the 2 periods), containing 55 g of total carbohydrates per test meal, and was purchased shortly after baking, every test day, at 8 AM.

On each test day in the two periods, subjects came to INTA between 07:30 h and 08:30 h, after an overnight fast of 12 hours Thirty minutes after installation of a catheter in a peripheral arm vein, 2 blood samples (3 ml) were taken at 15 min. intervals to obtain the baseline glucose and insulin values. Just after the second sampling (time 0), the white bread standard meal was ingested with 300 ml of water. Subsequently, blood samples (3 ml) were obtained at 15, 45, 60, 90, 120, 150 and 180 minutes, to measure glucose and insulin.

During the test period, the subjects were comfortably seated in a quiet room. They were not allowed to ingest foods before the end of the test. Mineral water without gas, calories or flavor was permitted to drink two hours after starting the test.

Blood samples were collected in tubes and centrifuged (4°C, 3,000 rpm for 15 min). Glucose was measured by the glucose-oxidase method (GOD-PAP) and insulin by RIA using commercial kits from DPC, Los Angeles, CA, USA, with intra-assay and inter-assay variation coefficients of 5.1 and 7.1%, respectively, and a sensitivity of 1.2 mIU/ml.

Statistical methods and data analysis

AUC for glucose and insulin (gAUC and iAUC) were calculated, according to the procedure of Wolofver & Jenkins, using serum glucose and insulin concentrations obtained before and during the 3 hour period following the meal.

The individual variability of gAUC and iAUC was calculated using the coefficient of variation (CV = 100 x SD/mean) for each subject. The mean value obtained for each subject was used to calculate the interindividual coefficient of variation. The same method was used to calculate the variability of gAUC and IAUC between subjects.

Statistical analyses were performed using Statistica for Windows version 4.5 (StatSoft Inc, Tulsa, OK, USA 1993). Descriptive data are expressed as mean ± standard deviation. Comparison between periods were done using student t-test.

The study was approved by the local ethics committee.

Results

Two male and eight female healthy volunteers participated in the study. Every one attended all the experiment days. The timing of the blood samples was strictly followed by the same research nurse that obtained the blood samples. Body mass index and baseline glucose an insulin values for each study period are shown in table I.

The mean AUCs of serum glucose during the two periods were similar. In the first period (3 studies/person) was 2,953.5 mg min/ml and ranged from 109.7 to 9,641.3 mg min/ml. In the second period, the mean AUC of glucose was 3,428.4 mg min/ml and ranged from 660.8 to 8,040 mg min/ml (table II).

The total intra-individual variation was 51.8%. In the first period it was 51.3% (range 24.9 to 91.4%) and 52.3% (range 25-91%) in the second period. The intra-individual variation in the complete study was 75.2%, in the first study period it was 61% and in the second period 90% (p = 0.45).
As a theoretical exercise, we calculated the ratio of the AUCs of the two study periods (period 2/period 1), this calculation corresponds to the glycemic index (GI) definition. The ratios ranged from 0.53 to 3.43, with a mean value of 1.42 ± 0.81 (GI: 53% to 343%).

The insulin AUC in the first period was 4,019.5 ± 1,663*180 min/ml and ranged between 1,677-6,823. The figures for the second period were 4,432.1 ± 2,502.2 uIU*180 min/ml, range 929-12,960 uIU*180 min/ml. The total intra-individual variation was 51.9%. In the first period it was 43.2% (range:7.7%-50.6%) and 60.6% (range 15%-103%), in the second period. The inter-individual variation in the complete study was 86%, 61% in the first period study and 111% in the second period (p = 0.45).

The ratio of the insulin AUCs between the two periods varied from 0.33 to 1.85, with a mean value of 1.03 ± 0.55 (II: 33%-185%).

**Discussion**

This study demonstrated that glucose and insulin response to a reference food, is not constant in the same healthy individual, when measured in a short interval, even being very rigorous with the methodology used. The same professionals participated in each study and the preparation of the standard meal was uniform.

Many authors have admitted that glycemic responses yielded by exactly the same test meal vary from day-to-day within subjects with a mean coefficient of variation between 56-25% in normal subjects.8 Wolover reported a CV fluctuating between 20 and 30% in a same subject, after consuming a glucose solution as a reference meal.7 Remarkably the inter-individual variation of the standard meal or a test food is high, but lower than the intra-individual variation. Thus, the reliability of the measure is not good, because within person variability is big when compared with the between person variability.9 This indicates that the glucose and insulin response is not only influenced by the meal composition, but also by other factors that may potentially influence de glycemic response. Probably, the differences between and within subjects in the AUC and GI of a food, are due to uncontrollable variables depending of each healthy individual, such as stress-induced changes in gastrointestinal motility and absorption rates, sleep deprivation that decreases insulin sensitivity in healthy subjects.10 As well, the composition of the meal consumed the prior 24-72 hours before the experiment or the degree of mastication that influences glucose absorption.11 Unfortunately we did not measure urinary catecholamine, and we only gave instructions about the last meal, but we did not provide the meal for the night before the study to our study subjects.

Another explanation for the high intra-individual variation of glucose AUC in this study, is that we measured blood glucose from a venous sample and not from a capillary sample. Wolover observed that the intra-individual variation was reduced from 57 to 23% by using capillary blood sample12 (Wolover, 2004). However Vrolix, did not observe significant differences in gAUC from capillary or venous blood glucose.13 Therefore there are not enough evidences to support that capillary blood samples are associated with lower within subject variation.

Most publications describe, in the methodology section, that standard food (white bread or glucose) was tested three times in each subject to minimize day to day variation, but they did not describe the within and between subject variation.

In clinical practice there are many examples of laboratory parameters, that we use as gold standards, that have an immense within and between subject variation. For example, the variation of the paired estimation of beta cell function by the Homeostasis Model Assessment (HOMA) is over 30%, indicating that it is not a good parameter to evaluate beta cell function. Moreover, the concordance between the hyperglycemic clamp (as the gold standard) and HOMA was low. More importantly, the authors that described the method concluded that the low precision of the model is a serious limit for its use. However, it is still universally employed as the method to estimate beta cell function in clinical practice.14

In consequence the low reliability of the glucose response or glycemic index to a given food, limits its clinical utility for individual dietary prescription.

**References**


| Table II  |

<table>
<thead>
<tr>
<th>Glucose and insulin area under the curve (AUC) of standard meal during the two periods</th>
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<tbody>
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<td>Glucose AUC</td>
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<td><strong>AUC</strong></td>
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<td>First Period</td>
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<td>Second Period</td>
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