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.1

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 stan-
dardization, should render a similar blood glucose
AUC and GI in the same or different individuals.5,6
However, in the clinical practice we, as other authors,
have observed that the inter-individual and intra-indi-
vidual variation of the GI is very high, independent of
the meal and the method of standardization.5,6
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 installa-
tion 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 comfort-
ably 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.

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 8040 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 in-
dividual 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).

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<th>Table I</th>
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<td>Baseline features of the study subjects</td>
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<td>Body Mass Index (weight/heigth²)</td>
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<td>Basal serum glucose (mg/dl)</td>
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<td>Basal serum insulin uIU</td>
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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 uIU*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. Wolover reported a CV fluctuating between 20 and 30% in a same subject, after consuming a glucose solution as a reference meal. 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. 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 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. 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. 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 sample (Wolover, 2004). However Vrolix, did not observe significant differences in gAUC from capillary or venous blood glucose. 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.

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


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