Nutrición Hospitalaria

Original

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

Sandra Hirsch, Gladys Barrera, Laura Leiva, María Pía de la Maza and Daniel Bunout

Institute of Nutrition and Food Technology (INTA). University of Chile. Santiago. Chile.

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.

(*Nutr Hosp.* 2013;28:541-544)

DOI:10.3305/nh.2013.28.2.6161

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

VARIABILIDAD DE LAS RESPUESTAS GLUCÉMICA Y DE INSULINA, INTRA E INTERSUJETO, A UNA COMIDA ESTÁNDAR EN INDIVIDUOS SANOS

Resumen

Objetivo: Evaluar la variabilidad inter e intra individual de la respuesta glicémica frente a la ingestión de un alimento estándar en sujetos sanos.

Material y métodos: Se midió en 6 oportunidades la respuesta glicémica e insulínica de un alimento estándar (pan batido blanco) en 10 voluntarios sanos. A cada sujeto se le midió la glicemia e insulina en ayuno a los 15, 45, 60, 90, 120, 150 y 180 minutos, después de ingerir el alimento estándar. Posteriormente se calculó el área bajo la curva (ABC) de glicemia e insulina en cada sujeto. Se calculó el coeficiente de variación intra e inter individual del ABC de glucosa e insulina.

Resultados: La variación intra-individual total del ABC de glucosa fue de 51,8% (rango: 24,9%-91,4%). La variación inter-individual del ABC de glucosa total fue 75,2%. La variación intra-individual del ABC de insulina fue de 51,9% (rango: 7,7%-103%). La variación inter-individual del ABC de insulina total fue de 86%.

Conclusión: La respuesta glicémica e insulínica a un alimento estándar tiene poca reproducibilidad, tanto intra e inter individual. En consecuencia, su utilidad clínica para la prescripción dietaria individual, está limitada.

(*Nutr Hosp.* 2013;28:541-544)

DOI:10.3305/nh.2013.28.2.6161

Palabras clave: *Respuesta glucémica. Respuesta insulínica. Variabilidad. Alimento estándar.*

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

Correspondence: Sandra Hirsch.
Institute of Nutrition and Food Technology (INTA).
University of Chile.
PO Box 138-11 Santiago. Chile.
E-mail: shirsch@inta.uchile.cl

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.[2,3,4] 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.[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/m^2, 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-

Table I
Baseline features of the study subjects

	First period	Second period
N	10	10
Body Mass Index (weight/heigth^2)	24.9 ± 2.9	24.3 ± 2.2
Basal serum glucose (mg/dl)	82.9 ± 4.7	82.3 ± 5.01
Basal serum insulin uIU	5.35 ± 3.24	6.02 ± 7.1

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 Wolever & Jenkins,[7] 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[R] 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 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 interindividual 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).

Table II
Glucose and insulin area under the curve (AUC) of standard meal during the two periods

	Glucose AUC		Insulin AUC	
	AUC mg·min/dl	Inter-individual variation %	AUC µUI·min/ml	Inter-individual variation %
First Period	2,953.3 ± 1,976.5	61	4,019.5 ± 1663	56.5
Second Period	3,428.4 ± 3,075.0	90	4,601.1 ± 5,120.5	111

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 sample[12] (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.[143]

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

1. Wolever TM, Jenkins DJ. The use of the glycemic index in predicting the blood glucose response to mixed meals. *Am J Clin Nutr* 1986; 43: 167-72.

2. Radulian G, Rusu E, Dragomir A, Posea M. Metabolic effects of low glycaemic index diets. *Nutr J* 2009; 29 (8): 5. Review.

3. Queiroz KC, Novato Silva I, de Cássia Gonçalves Alfenas R. Influence of the glycemic index and glycemic load of the diet in the glycemic control of diabetic children and teenagers. *Nutr Hosp* 2012; 27: 510-5.

4. Reis CE, Bordalo LA, Rocha AL, Freitas DM, da Silva MV, de Faria VC, Martino HS, Costa NM, Alfenas RC. Ground roasted peanuts leads to a lower post-prandial glycemic response than raw peanuts. *Nutr Hosp* 2011; 26: 745-51.

5. Gattás V, Barrera G, Leiva L, De La Maza Mp, Bunout D, Steenhout P, Klassen P, Voss T, Hirsch S. Glycemic and insulin indices of tube feeding formulas in healthy adults. *Rev Med Chile* 2007; 135: 879-84.

6. Wolever TM, Leung J, Vuksa V, Jenkins AL. Day-to-day variation in glycemic response elicited by white bread is not related to variation in satiety in humans. *Appetite* 2009; 52: 654-8.

7. Wolever TM, Jenkins DJ, Jenkins AL, Josse RG. The glycemic index: methodology and clinical implications. *Am J Clin Nutr* 1991; 54: 846-54.

8. Vega-Lopez S, Ausman LM, Griffith JL, Lichtenstein AH. Interindividual variability and intra-individual reproducibility of glycemic index values for commercial white bread. *Diabetes Care* 2007; 30: 1412-7.

9. Williams SM, Venn BJ, Perry T, Brown R, Wallace A, Mann JI, Green TJ. Another approach to estimating the reliability of glycaemic index. *Br J Nutr* 2008; 100: 364-72.

10. Trout DL, Behall KM, Osilesi O. Prediction of glycemic index for starchy foods. *Am J Clin Nutr* 1993; 58: 873-8.

11. Ranawana V, Monro JA, Mishra S, Henry CJ. Degree of particle size breakdown during mastication may be a possible cause of interindividual glycemic variability. *Nutr Res* 2010; 30: 246-54.

12. Wolever TM. Effect of blood sampling schedule and method of calculating the area under the curve on validity and precision of glycaemic index values. *Br J Nutr* 2004; 91: 295-301.

13. Vrolix R, Ronald P. Mensink. Variability of the glycemic response to single food products in healthy subjects. Contemporary Clinical Trials 2010; 31: 5-11.

14. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetología 1985; 28: 412-9.