Proposal for Insulinogenic Index (IGI)-Carbo70 as Experimental Evaluation for Diabetes

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Abstract

Background: The discussion has continued concerning Calorie Restriction (CR) and Low Carbohydrate Diet (LCD) for years. Authors and colleagues have continued clinical research on LCD. In this study, CR diet was given to diabetic patients and the new evaluation way of insulinogenic index-carbohydrate 70 g (IGI-carbo70) would be proposed.

Subjects and methods: The subjects were 48 patients with Type 2 diabetes mellitus (T2DM) and admitted for 14 days for further evaluation and treatment. CR diet was provided on day 1 and 2, including 60% carbohydrate, 25% lipids and 15% protein with 1400 kcal/day. On the morning of day 2, breakfast with 70 g of carbohydrate was given, and blood glucose and immune reactive insulin (IRI) at 0 and 30 min and IGI were investigated.

Results: Average HbA1c was 7.9% and Morbus (M) value was 108 in median. Glucose and IRI on 0-30 min significantly increased as 166-212 mg/dL, 4.3-1.9 μU/mL, respectively. Classified into 3 groups as to HbA1c level, low, middle and high group showed HbA1c 6.0%, 7.8%, 9.7%, respectively. Glucose and IRI on 0-30 min in median were 117-50, 166-203, 218-299 mg/dL, 4.4-12.8, 4.5-13.5, 4.2-9.9 μU/mL, with IGI 0.25, 0.14, 0.10, respectively.

Discussion and conclusion: Newly-proposed IGI-carbo70 was investigated, and there were several correlations among 8 related biomarkers. These findings suggest that current results would become the fundamental data and IGI-carbo70 could be the useful way to evaluate diabetic status by usual meal with mixed nutrients.

: (IGI-carbo70) Insulinogenic index-carbohydarate 70 g; (CR) Calorie restriction; (LCD) Low carbohydrate diet; (T2DM) Type 2 diabetes mellitus; (IRI) Immunoreactive insulin

A : IGI-carbo70: Insulinogenic Index-Carbohydarate 70 g; CR: Calorie Restriction; LCD: Low Carbohydrate Diet; T2DM: Type 2 Diabetes Mellitus; M value: Morbus value; MAGE: Mean Amplitude of Glycemic Excursions; IRI: Immunoreactive Insulin; VLCKD: Very Low-Carbohydrate Ketogenic Diet; CGM: Continuous Glucose Monitoring; HOMA-R: Homeostasis Model Assessment-Insulin Resistance; HOMA-β: Homeostasis Model Assessment of β-cell Function; HDL-C: High density Lipoprotein Cholesterol; LDL-C: Low Density Lipoprotein Cholesterol; 75 g OGTT: 75 g Oral Glucose Tolerance Test

The discussion has continued concerning Calorie Restriction (CR) and Low Carbohydrate Diet (LCD) for years [1-5]. Clinical predominance of LCD has been gradually known and more prevalent. In European and North American region, Atkins and Bernstein originally have begun to introduce LCD [6,7].

On contrast in Japan, the authors have started LCD, and reported thousands of cases with clinical efficacy [8,9]. Furthermore, we have investigated related research concerning 3 types of LCD formular meals, elevated ketone bodies, Morbus (M) value, lipid metabolism and renal function [10-12].

Through our clinical study, we always compared the differences of the glucose variability between CR and LCD. In this study, we have given CR diet to the patients with type 2 diabetes mellitus (T2DM), and investigated the responses of blood glucose, immunoreactive insulin (IRI) value and insulinogenic index (IGI), suggesting the usefulness of experimental application of IGI as an approach for clinical study.

The subjects enrolled in this study were 48 patients (M/F 23/25) with T2DM. They are 18-84 years old with 59.4 ± 12.9 (mean ± SD) years old in average, 60.5 years old in median value.

Subjects were admitted for 14 days for further evaluation and treatment of T2DM. The protocol of diet therapy was as follows: 1) Calorie Restriction (CR) diet was provided on days 1 and 2, which had 60% carbohydrate, 25% lipids and 15% protein with 1400 kcal/day. 2) Low Carbohydrate Diet (LCD) was provided from 3 to 14 days, which had 12% carbohydrates, 64% lipids and 24% protein with 1400 kcal/day. This is LCD has been so-called "super-LCD formula" in our clinical research for LCD, which is one of the very low-carbohydrate ketogenic diet (VLCKD) by the definitions of LCD [12-14].

Methods included the measurements of responses for glucose and IRI against 70 g of carbohydrate on the morning of day 2. CR diet has 840 kcal of carbohydrate per day, which equals totally 210 g of

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carbohydrate in 3 meals. en, breakfast including 70 g of carbohydrate was given to the patients a er overnight fasting, with the measurement of blood glucose and IRI on 0 min and 30 min. Other blood biomarkers were measured in fasting on day 2.

e content of CR diet is along the guideline of Japan Diabetes Society, in which PFC ratio is 14.7%, 26.9%, 58.4%, respectively [15]. is ratio has been stable from 1985 to 2015 on the national survey in Japan [16].

On day 2, daily pro le of blood glucose was studied 7 times a day, which are 8, 10, 12, 14, 17, 19, 22 h. According to the glucose level, 2 markers were calculated. One is the average glucose level, and another is Morbus (M) value. M value is a useful index representing both blood sugar level and mean amplitude of glycemic excursions (MAGE) [17-

children/adolescents [27]. As to T2DM with and without aggravation of parameters, IGI in average was showed 0.3 and 0.5, respectively [28].

Furthermore, IGI has been used a er a meal at 30 min [29-31]. e changes in IGI were correlated to the changes in the β-cell function in both normal glucose-tolerant and prediabetic individuals, which suggests it to be a valid proxy indicator for β-cell function in healthy individuals [29].

In Asian countries, overconsumption of starchy foods such as rice has induced a rapid and sharp postprandial hyperglycemia [32-34]. is increased glucose response is accompanied by an insulin surge and contributes to the etiology of diabetes [35].

Recently, e ect of co-ingestion of amino acids with rice on glycemic and insulin response was investigated in 7 various patterns [36]. Rice with 68 mL of amino acid mixture showed the best results in reducing the peak blood level [36]. Its merit lies in enabling people living in Asia to reduce postprandial hyperglycemia due to carbohydrate-rich rice meals by the inclusion of a ready-to-drink amino acid mixture [37-39].

A liquid mixed meal test was tried for the indices of insulin secretion in patients with diabetes [40]. Participants ingested 237 mL high protein boost-HP (Nestle) consisting of 33 g carbohydrate, 15 g protein and 6 g fat, (%Calories: 55% carbohydrate, 25% protein, and

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