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Response of Insulin Secretion to Small Amount of Meal on Low Carbohydrate Diet (LCD)

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Abstract

Diabetic nutritional therapy has been changing from Calorie Restriction (CR) to a Low Carbohydrate diet (LCD). Authors et al. have developed LCD medically and socially through the Japan LCD promotion association (JLCDPA), and proposed meal tolerance test (MTT) using LCD breakfast. For our research protocol, healthy subjects (n=8, M/F=4/4, BMI 20.5kg/m^2) received 75g oral glucose tolerance test (OGTT) and MTT, and changes in blood glucose and immunoreactive insulin (IRI) were measured. LCD meal included energy 307kcal, protein 13.8g, fat 23.9g, and carbohydrate 5.7g. The results from 0-30 min in average showed: i) 75gOGTT; 87.3-124.6mg/dL, 4.9-41.4μU/mL, ii) LCD; 90.3-84.3mg/dL, 5.4-12.2μU/mL, respectively. Decreased glucose may be from enough ability to secrete insulin to a glucose stimulus. These results would become reference data for future diabetic research.

Keywords: Low Carbohydrate diet, Japan LCD promotion association, Meal tolerance test, Immunoreactive insulin, Glycemic Index

Abbreviations: LCD: Low Carbohydrate Diet; JLCDPA: Japan LCD Promotion Association; MTT: Meal Tolerance Test; IRI: Immunoreactive Insulin; GI: Glycemic Index

Introduction

Diabetic patients have been increasing nowadays in the world(1). For recent diabetic therapy, standard treatment methods have been proposed by the American Diabetes Association (ADA), American College of Physicians (ACP), and others(2,3). There was an international mega investigation, which was Prospective Urban Rural Epidemiology (PURE) studies, including 140 thousand of diabetic patients from 18 countries. As a result, increased carbohydrate intake has brought a higher risk of total mortality with hazard ratio 1.28, associated with the recommendation of reduced carbohydrate intake(4).

Regarding diabetic nutritional therapy, there have been changes from Calorie Restriction (CR) to Low Carbohydrate diet (LCD). Historically speaking, Atkins and others have proposed LCD(5). After that, LCD has been popular for a wider area worldwide. In Japan, authors et al. have started LCD medically and socially through the Japan LCD promotion association (JLCDPA)(6). Three patterns of LCD were introduced, which are petite-LCD, standard-LCD, and super-LCD with a carbohydrate ratio of 40%, 26%, 12%, respectively(7). We have developed a social movement of LCD with various books, seminars, medical papers, and others(8).

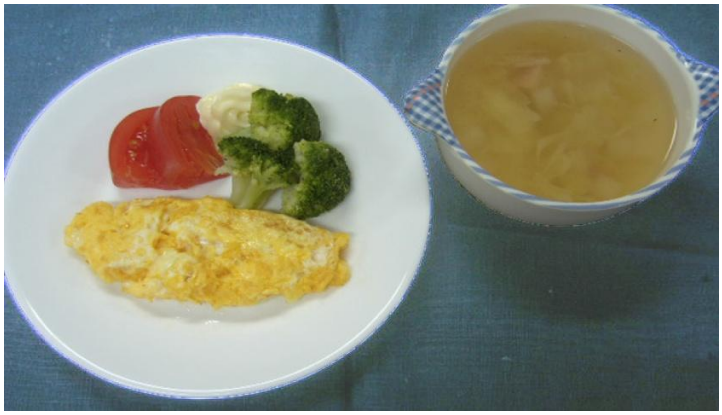
As we continued our clinical research on CR and LCD, a new index of an insulinogenic index (IGI) to carbohydrate 70g has been proposed(9). It was from the meal with carbohydrate 70g in the standard breakfast of CR(10). Continuing the direction of the meal tolerance test (MTT), we have developed current research, and describe in this report.

Research Protocol

In this study, subjects were enrolled who are healthy medical staff in the hospital with 24-32 years (n=8, male/female 4/4). They did not have any remarkable diseases or any health problems so far. Their body mass index (BMI) was 20.5 ± 1.5 kg/m^2 on average and any subject showed the BMI within a normal range.

Methods included two examinations for the subjects. One is the usual 75g oral glucose tolerance test (75gOGTT) with the measurements of blood glucose and insulin (immunoreactive insulin, IRI). Another exam is MTT. The content was the super-LCD meal, which the authors have initiated and developed for years. It has 307 kcal in energy, which has the same as that of 75gOGTT. The detailed content of the meal was that Omelet, broccoli, tomato, mayonnaise, and consommé soup with the nutritional elements of energy 307kcal, protein 13.8 g, fat 23.9 g, and carbohydrate 5.7 g (Figure 1).

Figure 1: Actual LCD for meal tolerance test (MTT) for breakfast



For these two protocols, 8 same subjects received twice tests of 75gOGTT and MTT. The detailed protocol of the endocrinological measurement included blood glucose (0 min, 30 min, 120 min) and IRI (0 min, 30min).

Statistical Analysis

In this study, measured data were shown by the mean and standard deviation. We have compared paired items for the obtained data in the parametric test. For evaluating the significant difference among the data of 0 min, 30 min, 120 min, paired t-test was applied(11).

Ethical Considerations

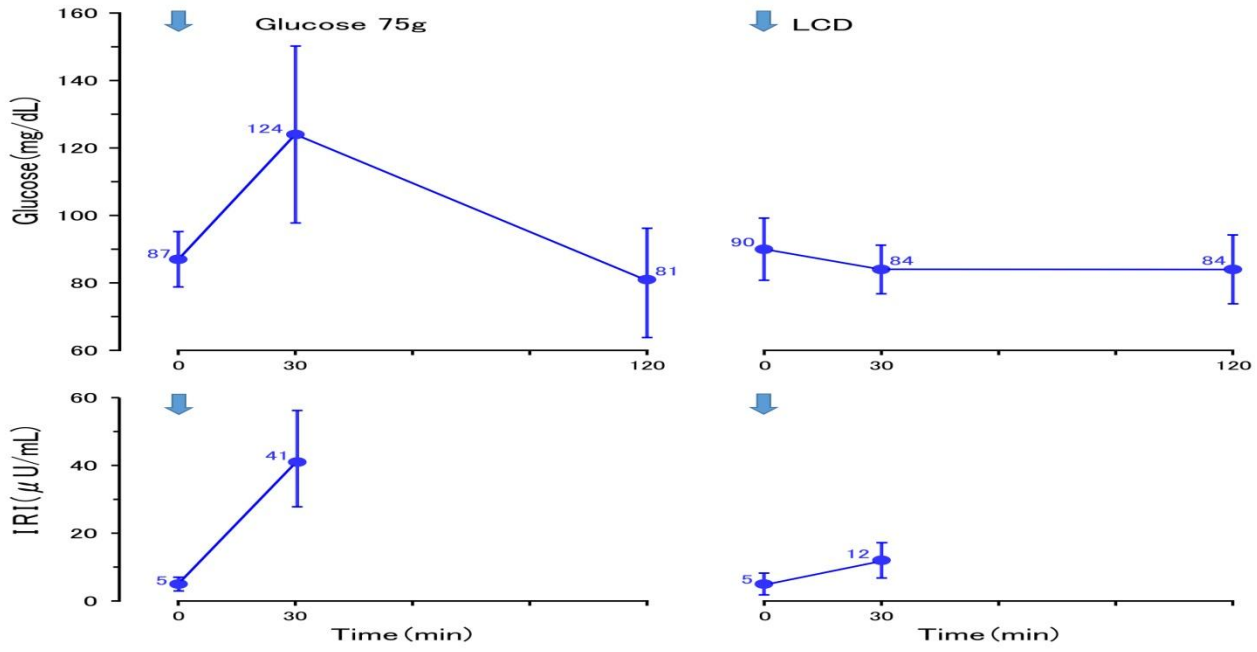
This investigation was basically conducted with the ethical principles of the Declaration of Helsinki. In addition, an additional comment was performed by the Ethical Guidelines for Research for Humans, associated with the concept of Good Clinical Practice (GCP). The author et al. established a related ethical committee, including the physician, nurse, pharmacist, nutritionist, and those of legal specialty. The discussion has continued with appropriate and valid manners and has decided to the agreements. The informed consent and written document agreements have been obtained from all subjects.

Results

1. **75gOGTT**

For 75gOGTT, blood glucose in 0 min, 30 min, 120 min was 87.3 ± 8.3 mg/dL, 124.6 ± 26.3 mg/dL, 80.8 ± 16.2 mg/dL, respectively. The value of IRI in 0, 30 min was 4.9 ± 1.6 μU/mL, 41.4 ± 14.7 μU/mL, respectively (Figure 2, left). Both values of glucose and IRI showed significant increase from 0 min to 30 min ($p<0.01$).

Figure 2: Responses of blood glucose and IRI for 75gOGTT and MTT
Left: 75gOGTT with carbohydrate 75g
Right: LCD meal with carbohydrate 5.7g by MTT



2. LCD

For MTT, blood glucose in 0 min, 30 min, 120 min was 90.3 ± 9.2 mg/dL, 84.3 ± 7.3 mg/dL, 84.3 ± 9.9 mg/dL, respectively. The value of IRI in 0, 30 min was 5.4 ± 2.6 μU/mL, 12.2 ± 4.7 μU/mL, respectively (Figure 2, right). Values of IRI not showed a significant increase from 0 min to 30 min ($p>0.05$). However, the values of glucose did not change statistically.

Discussion

The protocol meal (Figure 1) has been the standard LCD breakfast for research and practical use(7). It contains only carbohydrates 5.7g as an actual super-LCD menu. Super-LCD can be continued in our daily life by just excluding bread, rice, noodles, and so on(8). Such LCD movement in society has been spread through JLCDPA(6). In fact, since this meal contains only 5.7 g of sugars, it is expected that the increase in blood glucose after a meal will be very small.

The blood glucose and IRI responses to 75g OGTT (carbo 75g) and LCD (carbo 6g) showed impressive results (Figure 2). In Figure 2 left, blood glucose and insulin responses to OGTT were both normal responses. Subjects were the normal healthy not-obese younger generation, then the results were as expected. Regarding Figure 2 right, the insulin concentration was significantly increased at 30 min, probably because it was a normal person. At the same time, blood glucose on 30 min was lower than that of 0 min. Non-diabetic healthy subjects sometimes show lower post-prandial blood glucose levels after intake of LCD meal(8).

Furthermore, even patient with T2DM who is admitted to Takao Hospital and received detail diabetic evaluation sometimes shows the same phenomena(6). Such a case seems to be from the ability to secrete enough insulin in response to glucose stimulus who is in the mild level of diabetic status(8). From a pathophysiological point of view, hyperinsulinemia may give harmful influence to our body in normal subjects and diabetic patients(12). Intake of certain amount of glucose always results in hyperinsulinemia.

Originally, the Glycemic Index (GI) and Glycemic Load (GL) were described in 1980'(13). They can be useful for the influence of metabolic response from the ingestion of carbohydrates. Then, different glycemic responses (GR) were studied in various kinds of carbohydrates(13). There was a report of a systematic review of GI and GR from 2006 to 2018(14). They summarized that GI values from foods and diets did not seem to influence health outcomes or disease risks directly. Food patterns may be more involved in dietary guidance(14).

As for the results of GI and GL, lower values have contributed to the reduced risk of cardiovascular disease and diabetes(15). They investigated lots of kinds of breakfast, and reported that the average GI was 68.0 ± 9.2, and GL was 14.7 ± 3.1 g/30g weight(15).

For example, the GI of cooked rice varies significantly from 7 to 132 depending on the type of rice grain, cooking method, and processing method(16). Furthermore, the increase in blood glucose and IRI after intaking of white bread is significantly suppressed when protein is also ingested simultaneously(17).

Authors et al. have reported the response of blood glucose and insulin for 70g of carbohydrate in MTT study(18). Three group of T2DM patients (n=48) showed: HbA1c; 6.0 %, 7.8%, 9.7%, glucose and IRI on 0--30 min in median were 117--150, 166--203, 218--299 mg/dL, 4.4--12.8, 4.5--13.5, 4.2--9.9μU/mL, IGI

0.25, 0.14, 0.10, respectively(18). Thus, the new way of GTT was proposed, including 70g of carbohydrates from the usual breakfast of CR meal.

There are other types of MTT. One formula meal is high-protein Boost-HP with carbohydrate 33g, protein 15g, fat 6g(19). It contains 237ml of liquid with PFC ratio 25:20:55, made in Vevey, Switzerland. Another model is the international standard of the test meal(20). It is breakfast for MMT including 450kcal, salt 1.6g, and PFC = 15:35:50. This protocol includes 56g of carbohydrates.

The current study has some limitations. There were some papers on MTT with various conditions. As the included macronutrients vary with complex ratio, the speed of digestion and absorption would be different(21). Furthermore, both insulin and glucagon are involved in the exchange and regulation of blood glucose, which is also taken into consideration.

In summary, healthy subjects received two tests of GTT and MTT with measurements of glucose and IRI on 0 min and 30 min. For MTT, the standard formula of an LCD meal was used with 5.7g of carbohydrate. IRI responded from 5.4 U/ mL to 12.2 μU/mL. Further investigation will be expected concerning GTT in the future.

Conflicts of Interest: None.

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