Daily carbohydrate intake correlates with HbA1c in low carbohydrate diet (LCD).

Koji Ebe1,2*, Hiroshi Bando2,3, Kokoro Yamamoto1,2, Masahiro Bando4, Yoshikazu Yonei5

1Takao Hospital, Kyoto, Japan
2Low Carbohydrate Diet Promotion Association, Kyoto, Japan
3Tokushima University / Medical Research, Tokushima, Japan
4Department of Nutrition and Metabolism, Institute of Biomedical Sciences, Tokushima University Graduate School, Tokushima, Japan
5Anti-Aging Medical Research Center, Graduate School of Life and Medical Sciences, Doshisha University, Kyoto, Japan

Abstract

Background: There is an ongoing discussion about Low Carbohydrate Diet (LCD) and Calorie Restriction (CR). Authors and colleagues have initiated LCD in Japan, and reported clinical research studies on LCD and related biomarkers.

Subjects and Methods: Subjects were 51 patients with Type 2 diabetes mellitus (T2DM) with a mean age of 62.4 ± 6.9 years old. Patients were admitted for 14 days for treatment of super LCD formula, including 12% carbohydrates, 64% lipids, 24% protein with 1400 kcal/day. Six months later, the detail of meals for 7 days, HbA1c and lifestyle items were investigated.

Results: Subjects were classified into 2 groups according to the level of HbA1c at 7%. HbA1c was 6.1% vs 7.4%, and carbohydrate intake a day was 55.2g vs 123.6 g in group 1 and 2, respectively. Group 1 tended to have more usage of food and spice for LCD. There was significant correlation between HbA1c and carbohydrate intake (p<0.01).

Discussion and Conclusion: We adopted super LCD formula meal in this current study, including 12% of carbohydrate ratio. As to American Diabetes Association (ADA), carbohydrate intake per day in LCD would be less than 130g or less than 26% total energy per day. From our data, mild LCD might not be enough to maintain HbA1c less than 7%. Current results would be the fundamental data for LCD treatment for T2DM in the future.
2) After discharge from the hospital, they have regular visit in every 4 weeks on out-clinic. Six months later, we investigated the detail of meals for 7 days. The questionnaire included actual intake of meals, medicine, lifestyle, snacks, with some pictures of meals when needed. Authors and registered dieticians analyzed the carbohydrate amount by using the computer. According to HbA1c level, group 2 is subjects were classified into two groups: group 1 is ≤7% and 7% or greater. We have checked meal habit and the correlations between HbA1c and average carbohydrate intake per day.

3) Apart from the studies above, 2 cases were investigated in details out of 51 subjects. Case 1 is 70 year-old female, with M value calculated by daily profile of blood glucose 7 times a day. Case 2 is 70 year-old men, with daily profile of blood glucose all day for 7 days, using Continuous Glucose Monitoring (CGM) device.

**Glucose profile and M value**

During admission, daily profile of blood glucose was studied a day, which are 8, 10, 12, 14, 17, 19, 22h. It was measured on day 2 for CR and day 4 for LCD. According to the glucose profile, Morbus (M) value was calculated.

For years, M value has been a useful index showing blood sugar level and also mean amplitude of glycemic excursions (MAGE) [14-17]. As to the glucose variability, we measured daily profiles of blood glucose 7 times a day, and calculated average glucose level and M value. M value has been introduced and used for evaluating MAGE. M value is represented and calculated as a logarithmic transformation of the deviation of glycemia from an arbitrary assigned “ideal” glucose value. It expresses both the mean glucose value and the effect of glucose swings [14-18].

\[ M = \frac{MBS + MW}{2}; \quad M = \text{mean of MBSBS} \]

M value has been evaluated as follows: below 180 is normal and standard, 180-320 is borderline, and more than 320 is abnormal. There have been arguments about the adequate sampling times a day, with the precise evaluation of glucose variability and MAGE. The results on 7 times or 20 times a day were similar [14-17,19]. It showed the similar results in compared to the continuous glucose monitoring (CGM) [18,19,20].

**Statistical Analyses**

On this study, data were showed as the mean +/- standard deviation (SD) and represented as median, quartile of 25% and 75% in biomarkers.. When we investigate statistical analyses, correlation coefficients were calculated by using Pearson or Spearman test of the Microsoft Excel analytical tool [21]. Comparisons between the groups were made using the Wilcoxon rank sum test or the Bonferroni multiple comparison (Lambert method). We considered statistically significant, when the significance level was less than 5%.

**Ethical considerations**

We proceeded this study in compliance with the ethical principles. They are the Declaration of Helsinki and also Japan's Act on the Protection of Personal Information along with the Ministerial Ordinance on Good Clinical Practice (GCP) for Drug. The latter was from the Ordinance of Ministry of Health and Welfare No. 28 of March 27, 1997). We have no ethical committee meeting related to this research, and obtained informed consent from the subjects.

**Results:**

1. **HbA1c values**

Subjects were classified into 2 groups according to the level of HbA1c at 7%. Average HbA1c was 6.1% and 7.4%, respectively (Table 1). Average carbohydrate intake in each group was 55.2g and 123.6 g, respectively.

2. **Meal habit**

Both groups showed similar ratio of snack habits. The ratio of practical use of food and spice for LCD in daily life were higher in group 1 compared with group (Table 2).

3. **Carbohydrate intake per day**

There was significant correlation between HbA1c and
Table 1. HbA1c and carbohydrate intake of the subjects.

<table>
<thead>
<tr>
<th>Classifications</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c level (%)</td>
<td>&lt;7.0%</td>
<td>≥ 7.0%</td>
<td></td>
</tr>
<tr>
<td>number (n)</td>
<td>36</td>
<td>15</td>
<td>51</td>
</tr>
<tr>
<td>Hb1c (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>average</td>
<td>6.1</td>
<td>7.4</td>
<td>6.5</td>
</tr>
<tr>
<td>standard deviation</td>
<td>0.4</td>
<td>0.4</td>
<td>0.7</td>
</tr>
<tr>
<td>median</td>
<td>6.1</td>
<td>7.4</td>
<td>6.2</td>
</tr>
<tr>
<td>quartile 25%</td>
<td>5.8</td>
<td>7.2</td>
<td>5.9</td>
</tr>
<tr>
<td>quartile 75%</td>
<td>6.3</td>
<td>7.5</td>
<td>7.1</td>
</tr>
<tr>
<td>minimum</td>
<td>5.3</td>
<td>7</td>
<td>5.3</td>
</tr>
<tr>
<td>maximum</td>
<td>6.9</td>
<td>8.5</td>
<td>8.5</td>
</tr>
<tr>
<td>Carbohydrate intake (g/day)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>average</td>
<td>55.2</td>
<td>123.6</td>
<td>75.3</td>
</tr>
<tr>
<td>standard deviation</td>
<td>21.5</td>
<td>44.3</td>
<td>43.1</td>
</tr>
<tr>
<td>median</td>
<td>48.4</td>
<td>109.5</td>
<td>58.9</td>
</tr>
<tr>
<td>quartile 25%</td>
<td>41.8</td>
<td>89.5</td>
<td>44.8</td>
</tr>
<tr>
<td>quartile 75%</td>
<td>60.1</td>
<td>160.5</td>
<td>91</td>
</tr>
<tr>
<td>minimum</td>
<td>31</td>
<td>62.5</td>
<td>31</td>
</tr>
<tr>
<td>maximum</td>
<td>133.9</td>
<td>196.6</td>
<td>196</td>
</tr>
</tbody>
</table>

Table 2. Comparison of diet habits in 2 groups.

<table>
<thead>
<tr>
<th>HbA1c level (%)</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7.0%</td>
<td>25 (69%)</td>
<td>12 (80%)</td>
</tr>
<tr>
<td>≥ 7.0%</td>
<td>11 (31%)</td>
<td>3 (20%)</td>
</tr>
<tr>
<td>Snack habit (+)</td>
<td>18 (72%)</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>practical use of food for LCD (+)</td>
<td>7 (28%)</td>
<td>10 (83%)</td>
</tr>
<tr>
<td>practical use of spice for LCD (+)</td>
<td>31 (86%)</td>
<td>7 (47%)</td>
</tr>
<tr>
<td>practical use of spice for LCD (-)</td>
<td>5 (14%)</td>
<td>8 (53%)</td>
</tr>
</tbody>
</table>

carbohydrate intake per day (p < 0.01), shown in Figure 2. The regression curve showed y=42.547x - 200.9 with R²=0.4838.

4. Morbus value

Case 1 was 70-year-old female with HbA1c 8.9% on admission, who has 156 cm in height, 49kg in weight, 20.1 in body mass index (BMI) with no medication for T2DM. Changing from CR to LCD, daily profile of blood glucose and M value showed remarkable decrease in only 2 days (Figure 3).

5. Continuous glucose monitoring (CGM)

Case 2 was 70-year-old male with HbA1c 7.1%, who has 162 cm in height, 54 kg in weight, 20.6 in BMI with no medication for T2DM. He had super-LCD on Day 1,2,3,5,6,7, and formular CR diet on Day 4. Blood glucose profile due to continuous glucose monitoring (CGM) was shown in Figure 4, indicating that carbohydrate loading caused remarkable increase of daily profile of blood glucose.

Discussion

As for the development of LCD worldwide, Atkins, Bernstein and other researchers have contributed much in Western countries [1-7]. In Japan, Authors and colleagues have investigated and developed LCD in comparison with CR for years with clinical research studies [8-13]. We have also developed social movement, continuing the activity of Japan LCD Promotion Association with lectures and journals.

The content of CR diet was made according to the guideline of Japan Diabetes Society, in which PFC ratio is 14.7%, 26.9%, 58.4%, respectively [22]. This ratio has been almost the same from 1985 to 2015 on the national survey in Japan [23]. In general, PFC ratio has been 15:25:60.

On contrast, we proposed three patterns of LCD, which are super-LCD, standard- LCD and petit LCD. The carbohydrate ratio of these 3 types are, 12%, 26% and 40%, respectively. Our simple advice would be as follows: 1) super: avoid carbohydrate in 3 meals for super LCD, 2) standard: avoid carbohydrate in 2 meals, 3) petit: avoid carbohydrate in only supper. These are easily understood and continued for everyone.

Current study revealed two important results as follows: 1) there was a significant difference of carbohydrate intake in 2 groups, which are 55 g vs. 124 g per day, and 2) subjects in group 1 usually pay attention to using foods and spices connected to LCDs.

As for the recommendation from American Diabetes Association (ADA), carbohydrate intake per day would be less than 130 g or less than 26% total energy per day [6,24]. However, taking our results into consideration, this is not enough to maintain HbA1c less than 7%.

Meal habits are different in Western and Asian countries. In the latter, they usually have overconsumption of starch foods such as rice and crops, inducing a sharp and rapid postprandial hyperglycemia [25-27]. By this glucose response, an insulin surge would contribute to the etiology of diabetes [28].

Effect of co-ingestion of amino acids with rice on glycemic response was recently studied, and rice and amino acid mixture revealed the best results in decreasing the peak blood level [29]. By usage of this way, Asian people can reduce postprandial hyperglycemia due to carbohydrate-rich rice meals [30-32].

The effect of Japanese rice bowl topped with beef to blood glucose was investigated. It includes protein 18.4 g, fat 20.9 g and carbohydrate 82.9 g [33]. After it was given to 12 volunteers of 26 years old in average, blood glucose was increased 65 mg/dL in 30 min. Consequently, even if the subjects are young and healthy, blood glucose showed remarkable increase by intake of rice.

In association with report above [33], one of the limitation of this study would be the subjects including only Japanese with the characteristic meal habit taking considerable carbohydrate such as rice and noodle.

There has been a large-scale epidemiological study, “The Prospective Urban Rural Epidemiology (PURE) study”. It included 140 thousands subjects in 600 communities from 17-18 countries around the world [34,35]. By studying fats and carbohydrate intake, higher carbohydrate intake with an increased risk of total mortality (HR 1.28) were observed. Then, lower intake of carbohydrate would be recommended [36,37].

Recently, International Diabetes Federation (IDF) showed the problems worldwide [38], in which diabetes, obesity and metabolic syndrome (Met-S) have been increasing, and diabetic prevalence will be increasing from 8.8% in 2015 to 10.4% in 2040 [39,40]. IDF summarized Standards of Medical Care in Diabetes in 2015 [41]. In this guideline, monitoring carbohydrate intake, carbohydrate counting and experience-

Figure 2. Correlation between HbA1c and Carbohydrate intake per day. There are significant correlation between HbA1c and carbohydrate intake per day (p<0.01). According to the value of HbA1c, subjects were classified into group 1 (HbA1c<7.0%) and group 2 (HbA1c ≥ 7.0%). Blue round plots represent group 1, and red square plots represent group 2.

Figure 3. Case 1 with M value investigation. Case 1 was 70 year-old female with HbA1c 8.9%, who has 156 cm in height, 49 kg in weight, 20.1 in body mass index (BMI) with no medication for T2DM. As the meal changed from CR to LCD, blood glucose and M value decreased remarkably in only 2 days.

Figure 4. Case 2 with continuous glucose monitoring (CGM) investigation. Case 2 was 70 year-old male with HbA1c 7.1%, who has 162 cm in height, 54 kg in weight, 20.6 in BMI with no medication for T2DM. He had super-LCD on Day 1,2,3,5,6,7, and formular CR diet on Day 4. (LCD; low carbohydrate diet, CR; calorie restriction)
based estimation would be crucial. Continuous investigation of eating patterns and macronutrient distribution would lead to achieving glycemic control in the future.

Conclusions

Significant correlation between HbA1c and carbohydrate intake per day was shown, indicating the efficacy of LCD. Furthermore, mild LCD about less than 130 g of carbohydrate per day seemed not be enough to maintain HbA1c less than 7%. Current results would become the fundamental data for LCD treatment for T2DM in the future.

Acknowledgements

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Conflicts of Interest

The authors have no conflicts of interest.

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*Correspondence to:
Hiroshi Bando
Tokushima University /Medical Research
Nakashowa 1-61, Tokushima 770-0943
Japan
Tel: +81-90-3187-2485
E-mail: pianomed@bronze.ocn.ne.jp