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ORIGINAL RESEARCH

Changes in Body Weight, Dysglycemia, and Dyslipidemia After Moderately Low-Carbohydrate Diet Education (LOCABO Challenge Program) Among Workers in Japan

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Purpose: It is theorized that the prevalence of obesity has not decreased owing to poor adherence to implemented programs addressing metabolic syndrome, obesity, and diabetes in Japan. Therefore, we intended to evaluate the influence of a moderately low-carbohydrate diet on improving markers of metabolic syndrome among workers in Japan.

Patients and Methods: Participants with metabolic syndrome or obesity were recruited based on the eligibility criteria for the Specific Health Guidance program and educated on a moderately low-carbohydrate diet between spring 2016 and fall 2018. The participants were then made to report their food intake and body weight once a week for the next 12 weeks and were counselled on maintaining a moderately low-carbohydrate diet. HbA1c levels, lipid profile, body weight, and sleep quality were evaluated. The normality of the data was evaluated using the Skewness/Kurtosis test. Each variable was compared before and after the intervention using the Wilcoxon signed-rank test. Further, a subgroup analysis of the data from the participants whose variables were abnormal at baseline was performed.

Results: Among the 101 enrolled participants, a decrease in the median weight (from 82.5 to 79.7 kg, $p<0.001$, n=46), body mass index (from 27.3 to 26.9 kg/m^2, $p<0.001$, n=46), and apnea-hypopnea index (from 24.1 to 17.1, $p<0.01$, n=39) was observed. Subgroup analysis of participants with abnormal baseline values revealed changes in HbA1c (from 6.7% to 5.8%, $p<0.001$, n=34), total cholesterol (from 220 to 209 mg/dL, $p<0.01$, n=54), low-density lipoprotein cholesterol (from 133 to 120 mg/dL, $p<0.001$, n=31), high-density lipoprotein cholesterol (from 35 to 40 mg/dL, $p<0.01$, n=31), triglycerides (from 242 to 190 mg/dL, $p<0.01$, n=57), and deep sleep percentage (from 10.4% to 18.2%, $p<0.05$, n=7).

Conclusion: A moderately low-carbohydrate diet may be considered a potential intervention for improving the markers of metabolic syndrome, obesity, and diabetes.

Keywords: metabolic syndrome, moderately low-carbohydrate diet, obesity, overweight, Japan

Introduction

Metabolic syndrome (MetS), obesity, and diabetes are simultaneous global epidemics.[1,2] Previous studies have suggested that lifestyle interventions can effectively reduce body weight, prevent the onset of diabetes, and improve blood pressure and lipid profile.[3–7] In Japan, the Ministry of Health, Labour and Welfare started the Specific Health Checkup and Specific Health Guidance projects

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in 2008 to reduce and/or treat MetS.[8] The Specific Health Checkup includes annual laboratory tests, questionnaire-based health assessments, and physical examination to evaluate MetS risk. The Specific Health Guidance includes advice on energy restriction and physical activity (see Supplementary Materials) and was developed for high risk participants. As these interventions are recognized as complicated and challenging to adhere to, face-to-face individual behavioral counseling is recommended.[9] Although preliminary evaluation studies have reported that the participants of the Specific Health Guidance program achieved body weight reduction (on average, 1.98 kg for men and 2.25 kg for women) and improvement in plasma glucose, blood pressure, and lipid profile;[10,11] a recent large-scale evaluation revealed no association between the Specific Health Guidance and clinically meaningful weight loss or improvement of other cardiovascular risk factors.[12] The Specific Health Guidance involves lifestyle interventions such as energy restriction and encouragement of physical activity, which are perceived as troublesome and difficult to maintain.[13,14] This suggests that novel methods of effective implementation are needed.[11,15] Therefore, we developed a novel 3-month intervention program, consisting of non-energy-restricted moderately low-carbohydrate diet education only.[16] We named the diet (roughly 70–130 g/day of carbohydrate intake) LOCABO, and the evaluation program the LOCABO challenge. LOCABO has a target carbohydrate content of 20–40 g per meal. Furthermore, consuming confectionary amounting to 10 g of carbohydrates per day was permitted, resulting in a total carbohydrate intake goal of 70–130 g/day.[16–18]

Recently, Hyde et al compared low (45 g/day), moderate (234 g/day), and high (420 g/day) carbohydrate diets in a 4-week crossover study. In this feeding trial, a low-carbohydrate diet appeared superior to a moderate- and high-carbohydrate diet at reversing MetS.[19] However, Johnston et al have reported that a ketogenic diet (<50 g/day of carbohydrates) yields no metabolic advantage over a non-ketogenic low-carbohydrate diet.[20] Although the reasons for the difference between these two studies are unclear, one of these may be the difference in the study design: one was a feeding study[19] and the other did not include feeding.[20] In fact, Harvey et al have reported that adherence to the allocation of carbohydrate was more easily achieved in moderately low-carbohydrate diet and low-carbohydrate diet groups compared to the ketogenic diet group.[21] Furthermore, Li and Heber commented that following a ketogenic diet requires the supervision of a physician and a registered dietitian.[22] Given these considerations, we decided to retain the carbohydrate intake within a lower limit to prevent ketogenesis (>20 g/meal) and remain consistent with the definition of a low-carbohydrate diet (<130 g/day).[23,24] The aim of this study was to evaluate the influence of the LOCABO challenge on improving the markers of MetS. To the best of our knowledge, this is the first study to evaluate the influence of moderately low-carbohydrate diet education incorporated into an intervention for MetS traits, such as overweight, dysglycemia, and dyslipidemia, in Japan. As MetS has also been known to have a bidirectional relationship with sleep apnea,[25] we also evaluated sleep quality in this study.

Patients and Methods

Participants

This was a 12-week interventional cohort study. The study cohort was recruited from two companies, Hinomaru Kotsu Co. Ltd, which is one of the largest taxi companies in Tokyo, and Lawson Inc., one of the largest convenience store chains in Japan. As an interventional method similar to the Specific Health Guidance, the companies adopted the LOCABO challenge for their taxi drivers and convenience store staff. Recruitment took place twice per year, and each round enrolled 10–30 participants. The upper limit on the number of participants (30) was set based on our capacity to maintain effective communication between the participants and study staff. Between spring 2016 and fall 2018, a total of six recruitment rounds took place, involving taxi drivers and convenience store staff who are shift workers and had difficulty in maintaining regular eating and exercise habits. The participating companies identified workers who were interested in the LOCABO challenge through office posters and intranet magazines. They were then included in the study based on the eligibility for the Specific Health Guidance program. To eliminate the effect of medication on the study results, subjects who took antidiabetic and antihyperlipidemic drugs were excluded from this study. The inclusion criteria of this study has been detailed separately and provided as Supplementary Materials. This study was approved by the Institutional Review Board of the Kitasato Institute Hospital (Approval Study No. 18049). The study was performed in accordance with the Declaration of Helsinki. All participants were informed about the risks, benefits, and aims of the LOCABO challenge and were informed that they could withdraw at any time without any consequence. To prevent pressure from employers, participants provided their consent as part of their first food intake record.

Sample Size Calculation

Based on the findings of our previous study, we anticipated a change in HbA1c level of 0.6±0.0% in participants with diabetes.[16] Furthermore, we anticipated a dropout rate of 20%. Considering these factors, we required 92 participants, while ensuring that the study meets the following parameters: $\alpha = 0.05$, power = 0.90, and correlation = 0.40. Therefore, we decided to recruit participants over 3 years (6 enrollment rounds), from spring 2016 to fall 2018.

Education Schedule

The LOCABO challenge began with an on-site seminar about the effectiveness, safety, and dietary pattern of the LOCABO diet. In this 60-minute seminar, we explained to the participants the burden of diabetes and MetS, showed them the results of our previous trial,[16] and discussed food selection, including introducing restaurants that had LOCABO-compliant menus. Subsequently, participants were asked to record their food intake and body weight self-measurements and either email or fax these records to the study team every week for 12 weeks. The study team subsequently reviewed the participants' records and responded with comments or suggestions on the same sheet, within 3 days. The participants were advised to maintain their habitual physical activity and asked not to initiate any medication for diabetes and hyperlipidemia during the 12-week study period. Details of the seminar can be found in the Supplementary Materials, and the design of the study in the Figure 1.

Measurement and Evaluation of Variables

At the first and final session, we prepared a Specimen Measurement Office,[26] where we measured participants' hemoglobin (Hb) A1c and lipid profile (Cobas b101, Roche Diagnostics Japan, Tokyo) using fresh capillary blood. We evaluated the change in HbA1c and lipid profile (total cholesterol [TC], low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], and triglycerides [TG]) of all the participants. We evaluated the body weight and BMI data of the 46 participants who allowed to measure their body weight at baseline and in the final session. Furthermore, in trials conducted in 2016, we introduced a home-based sleep apnea test using a sleep-monitoring machine (WatchPAT, Philips Japan, Inc., Tokyo). WatchPAT can continuously measure oxygen saturation through pulse oximetry (SpO_2) and sleep stage through heart rate, and thus, is able to evaluate the apnea-hypopnea index (AHI), the lowest SpO_2, and deep sleep percentage. The reliability of WatchPAT is well established.[27] In this study, we did not

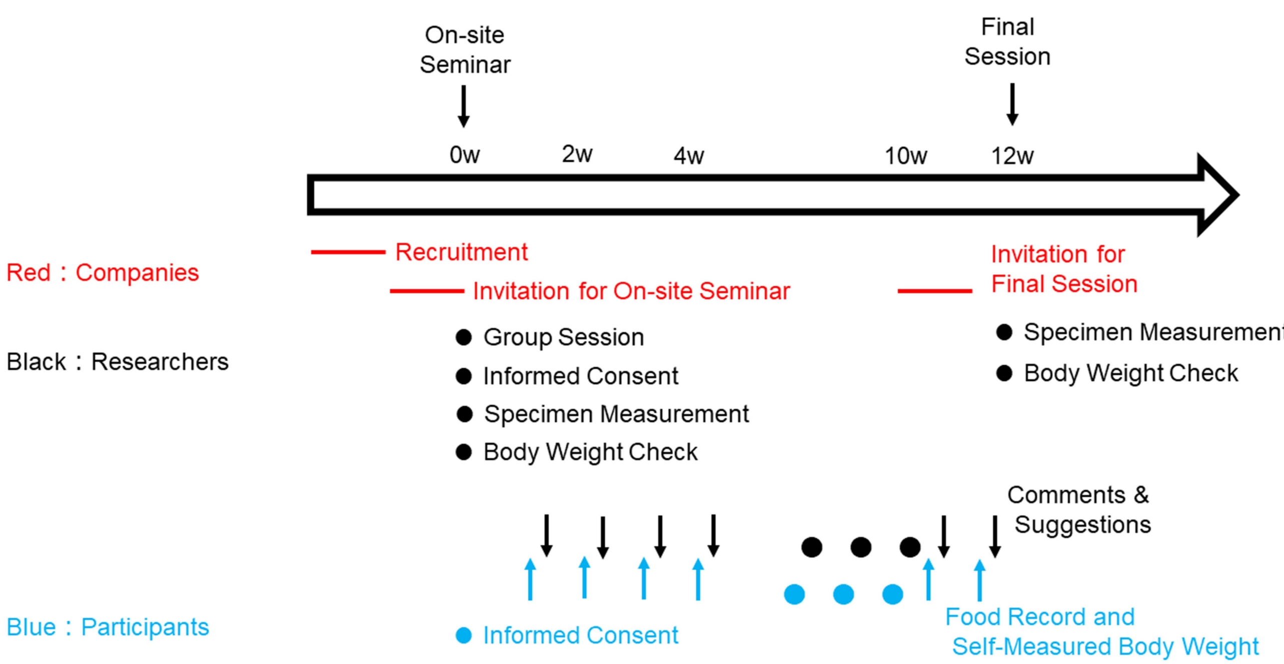

Figure 1 Schematic study design. Each participant provided a record of the food consumed by them and the researchers responded to them with comments and suggestions every week during the study period.

calculate energy and macronutrients intake using food record and did not evaluate adherence to LOCABO because our education to limit carbohydrate intake was not an aim but was rather a method to improve subjects' outcome.

Statistical Analysis

The normality of the data was evaluated using the Skewness/Kurtosis test. Since all variables except LDL-C were not normally distributed, we compared each variable before and after intervention using the Wilcoxon signed-rank test. For each variable, statistical procedures were based on complete before and after values. We performed a subgroup analysis of the data from the participants whose variables were abnormal at baseline: HbA1c ≥6.0% or ≥5.6%, TC ≥200 mg/dL, LDL-C ≥120 mg/dL, HDL-C <40 mg/dL, TG ≥150 mg/dL, BMI ≥25 kg/m^2, AHI score ≥5, lowest SpO2 <90%, and deep sleep percentage <13%. We performed statistical analysis using STATA version 13 (StataCorp LLC, TX, USA). The significance level for statistical tests was set at $p<0.05$.

Results

Blood Tests

We enrolled 101 participants during 2016–2018. No adverse event or change in medication was reported during the LOCABO challenge. The results of the whole cohort are shown in Table 1. There were no significant changes in any of the variables of interest (HbA1c, TC, LDL-C, HDL-C, and TG). However, subgroup analysis of the data from the participants whose variables were abnormal at baseline revealed significant changes in all variables of interest (Table 2). In particular, participants with HbA1c ≥6.0% at baseline showed a reduction in median HbA1c from 6.7% to 5.8% (z=3.958; p=0.0001).

Anthropometric Measurements

The median body weight and BMI reduced from 82.5 kg and 27.3 kg/m^2 to 79.7 kg and 26.9 kg/m^2 (z=4.628 and z=4.645; p<0.0001), respectively (Table 1). The mean body weight change was 3.55 ± 4.42%, with a median of 3.64% (quartile range 5.68–0.77%) reduction. Among the participants with a BMI ≥25 kg/m^2 at baseline, the average body weight and BMI reductions were comparable with the reduction reported for the whole cohort (Table 2).

Sleep Study

The 2016 sleep study involved 40 participants. Data from one participant could not be included due to problems with equipment. Thus, data from 39 participants were evaluated, revealing a significant change in the AHI score (from 24.1 to 17.1, z=2.610; p=0.0091) (Table 1). When we selected participants with abnormal values at baseline, statistical analysis also revealed a significant improvement in the deep sleep percentage (from 10.4% to 18.2%, z=2.366; p=0.018) (Table 2).

Table 1 Measurements Before and After 12 Weeks of Following a Moderately Low-Carbohydrate Diet (Median [Quartile])

Biomarker	Baseline	End of Study	*p*-value*
Blood Test (n=101)			
HbA1c (%)	5.7 (5.4–6.0)	5.6 (5.4–5.9)	n.s. (0.39)
TC (mg/dL)	203 (182–222)	198 (168–219)	n.s. (0.054)
LDL-C (mg/dL)	106 (93–126)	106 (86–129)	n.s. (0.11)
HDL-C (mg/dL)	48 (38–61)	47 (39–59)	n.s. (0.14)
TG (mg/dL)	178 (117–278)	157 (114–236)	n.s. (0.73)
Body Weight (n=46)			
Body weight (kg)	82.5 (72.8–88.0)	79.7 (71.9–85.9)	<0.001
BMI (kg/m^2)	27.3 (25.9–28.8)	26.9 (24.8–28.6)	<0.001
Sleep Study (n=39)			
Apnea-hypopnea index	24.1 (10.6–40.9)	17.1 (8.2–28.8)	<0.01
Lowest SpO2 (%)	84 (78–88)	84 (79–88)	n.s. (0.24)
Deep sleep percentage (%)	17.0 (15.4–22.7)	19.1 (15.2–24.0)	n.s. (0.73)

Note: *Wilcoxon signed-rank test.
Abbreviations: TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; SpO2, oxygen saturation through pulse oximetry; n.s., non-significant.

Table 2 Measurements Before and After 12 Weeks of Following a Moderately Low-Carbohydrate Diet in the Subgroup with Abnormal Results at Baseline (Median [Quartile])

Biomarker	Baseline	End of Study	*p*-value*
Blood Test			
HbA1c (%) (≥6.0) (n=34)	6.7 (6.0–7.6)	5.8 (5.5–6.3)	<0.001
HbA1c (%) (≥5.6) (n=60)	6.0 (5.7–6.8)	5.6 (5.5–6.0)	<0.001
TC (mg/dL) (≥200) (n=54)	220 (206–230)	209 (192–225)	<0.01
LDL-C (mg/dL) (≥120) (n=31)	133 (125–149)	120 (102–136)	<0.001
HDL-C (mg/dL) (<40) (n=31)	35 (30–38)	40 (33–44)	<0.01
TG (mg/dL) (≥150) (n=57)	242 (191–367)	190 (134–285)	<0.01
Body Weight (BMI >25) (n=37)			
Body weight (kg)	85.0 (80.5–89.7)	83.0 (77.2–87.0)	<0.001
BMI (kg/m^2)	28.0 (26.7–30.4)	27.2 (25.7–28.7)	<0.001
Sleep Study			
Apnea-hypopnea index (≥5) (n=34)	25.1 (13.9–41.6)	17.2 (11.8–28.8)	<0.01
Lowest SpO2 (%) (<90) (n=34)	84 (78–86)	84 (79–88)	n.s. (0.16)
Deep sleep percentage (%) (<13) (n=7)	10.4 (0–12.2)	18.2 (13.0–22.2)	<0.05

Notes: *Wilcoxon signed-rank test.
Abbreviations: TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; SpO2, oxygen saturation through pulse oximetry; n.s., non-significant.

Discussion

Previously, Riccardi and Rivellese proposed low-saturated fat, low-carbohydrate, and low-glycemic index diets for the dietary treatment of MetS.[28] Although recent American Heart Association guidelines recommend the replacement of saturated fat,[29] several studies have described that the replacement of saturated fat with carbohydrates is associated with no improvement or even an increase in cardiovascular risk.[30–32] Furthermore, a low-fat diet is recognized as a meaningless intervention for cardiovascular disease risk management.[33] Thus, we evaluated a low-carbohydrate diet in this study. Furthermore, we did not adopt a ketogenic diet. Although Saslow et al have reported a ketogenic diet to be superior in comparison with a moderately low-carbohydrate diet,[34,35] there are several reports of ketoacidosis in subjects without diabetes who follow a ketogenic diet.[36–39] Following a ketogenic diet requires the supervision of a physician and a registered dietitian.[22] Thus, we adopted LOCABO.

In this study, LOCABO was associated with improving body composition and AHI scores. In addition, the HbA1c, lipid profile, and deep sleep percentage improved in participants with abnormal values at baseline. Importantly, for participants whose values of the aforementioned biomarkers were abnormal at baseline, the means of the post-intervention results for HbA1c, LDL-C, HDL-C, and deep sleep percentage were all within the normal range, suggesting both a significant and a clinically relevant change. According to a previous report,[40] a 2–4% body weight reduction corresponds to a 4–6 mmHg reduction in systolic and diastolic blood pressure. Although this study did not measure blood pressure, it is theorized that the 3.55 ± 4.42% body weight reduction reported in this study may correspond to a proportional blood pressure reduction. These observations suggest that LOCABO is an effective method to treat and/or prevent MetS among Japanese workers.

The reason for stagnation in MetS prevalence in Japan is thought to be low participation in the Specific Health Guidance program.[8–10,12] In our study, although the questionnaire was not an established one and the data were not shown, 50% of the participants felt that it was easy to follow LOCABO, while 68% found it easier to follow it compared to other dietary approaches they had previously attempted. These findings suggest that LOCABO is a suitable method for improving participation in the Specific Health Guidance program.

Recently, one Iranian group reported the association of low-carbohydrate diet score with cardiovascular risk factors and sleep status.[41,42] According to this group, although low-carbohydrate diet score did not show statistically significant association with cardiovascular risk factors,[41] there were associations with better sleep status.[42] However, since their study had a cross-sectional design, further research will be needed to validate their findings.

The strength of our study is that this is the first study to show the influence of LOCABO in improving the biomarkers of MetS in Japan. Previously, a low-carbohydrate diet has been shown to improve glycemia.[43] However, few studies to date have evaluated the effect of a low-carbohydrate diet on the risk of developing MetS or diabetes.[44] To the best of our knowledge, this is the first study to evaluate the influence of moderately low-carbohydrate diet education on these outcomes in Japan, as well as to report the influence of LOCABO on sleep apnea and sleepiness. Recently, Shinoda et al have reported a 73.5% prevalence of sleep apnea in Japanese individuals with a BMI of 20–25 kg/m^2, and an 86.5% prevalence in Japanese individuals with a BMI of 25–30 kg/m^2 who also had diabetes.[45] In our cohort (median BMI: 27.3 kg/m^2), 34 among 39 (87.1%) participants had sleep apnea (AHI score >5). Although MetS and diabetes are different conditions, their prevalence was similar in the present study.[45] In the present cohort, the AHI score significantly improved (median change from 24.1 to 17.1), consistent with the improvement reported in a previous meta-analysis, where it was 6.04 in seven randomized clinical trials and 12.26 in nine before-after studies.[46] To assess the changes in SpO_2 and deep sleep percentage accurately, studies with larger samples are required to allow for age- and gender-stratified analysis.[47]

This study has some limitations. First, there was no control group; thus, we cannot exclude the possibility that factors other than LOCABO, such as counseling alone, also affected the results. Second, the sample size in the sub-analysis was small. Third, the participants had to apply to enroll in the study; this could have introduced a selection bias in the study sample because individuals who were more motivated to achieve changes in body weight, dysglycemia, and dyslipidemia, than the general population who were likely to enroll in the Specific Health Guidance program. However, 68% of participants felt that it was easier to follow LOCABO than other dietary approaches. In fact, we recently reported that LOCABO could maintain its effect on HbA1c improvement over 36 months[17] and that even Michelin-star restaurants could serve moderately low-carbohydrate menus.[48] These studies have shown that adherence to LOCABO may be relatively easy and that it may confer long-term health benefits. Selection bias is unlikely to have significantly affected the data, in particular, for the groups involving taxi drivers and convenience store staff. Fourth, the study duration of 12 weeks is short and we cannot rule out the seasonal change. The achievement rates of HbA1c, blood pressure, and LDL cholesterol were lowest in winter and highest in summer.[49] We recruited participants in spring and fall in this study. Thus, the influence of seasonal change must be limited. Finally, our study findings might have limited generalizability. In this study, dietary education was delivered by SY, who is accustomed to delivering low-carbohydrate diet education. However, in Japan, the majority of registered dietitians are not accustomed to it. Furthermore, Sato et al reported that weight reduction achieved with a moderately low-carbohydrate diet at 6 months was not maintained at 12 months.[50,51] However, other studies have shown long-term improvement as a result of a moderately low-carbohydrate diet at 24[52] and 36 months.[17] Furthermore, a systematic review of studies involving patients with type 2 diabetes in Japan revealed that a moderately low-carbohydrate diet was superior to an energy-restricted diet.[53] Thus, it is important that registered dietitians in Japan are able to adequately provide low-carbohydrate diet education.

Conclusion

LOCABO could be a potential intervention method for preventing and treating MetS. Japanese companies, health insurance associations, registered dietitians, and health care providers should recognize that consumption of a moderately low-carbohydrate diet could be a potential method to improve markers of health associated with MetS. Nevertheless, to confirm the present study findings, randomized clinical trials that compare the effects of a moderately low-carbohydrate diet and an energy restriction-based diet on MetS are needed.

Ethics Approval and Informed Consent

This study was approved by the Institutional Review Board of the Kitasato Institute Hospital (Approval Study No. 18049) and was performed in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants involved in the study.

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Disclosure

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