



East Asian diet-mimicking diet plan based on the Mediterranean diet and the Dietary Approaches to Stop Hypertension diet in adults with type 2 diabetes: A randomized controlled trial

Sang-Man Jin¹ , Jiyeon Ahn², Jiyun Park¹, Kyu Yeon Hur¹, Jae Hyeon Kim¹, Moon-Kyu Lee^{3*} 

¹Division of Endocrinology and Metabolism, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, ²Division of Endocrinology and Metabolism, Department of Internal Medicine, Hanyang University College of Medicine, Myongji Hospital, Goyang, Korea, and ³Division of Endocrinology and Metabolism, Department of Internal Medicine, Soonchunhyang University Gumi Hospital, Soonchunhyang University School of Medicine, Gumi, Korea

Keywords

Diabetes mellitus, Mediterranean diet, Asians

*Correspondence

Moon-Kyu Lee
Tel.: +82-54-468-9046
Fax: +82-54-468-9051
E-mail address:
leemk4132@gmail.com

J Diabetes Investig 2021; 12: 357–364

doi: 10.1111/jdi.13384

Clinical Trial Registry

Clinical Research Information Service
KCT0002217

ABSTRACT

Aims/Introduction: Using an investigational diet plan based on the Mediterranean diet and the Dietary Approaches to Stop Hypertension diet comprised of substitute ingredients that mimic the average East Asian diet, this study assessed the glycemic benefits in comparison with a food exchange system-based diet in established type 2 diabetes patients.

Materials and Methods: This was a 12-week, open-label randomized clinical trial carried out among 60 Korean adults with type 2 diabetes having a median body mass index of 23.5 kg/m². Glycemic benefits in the investigational diet (group A) were compared with those obtained with a food exchange system-based diet, either in the form of ready meals provided to participants (group B) or not (group C). The primary end-point was changes in glycosylated hemoglobin from baseline to week 12.

Results: Changes in glycosylated hemoglobin (%) from baseline to week 12 were -0.97 ± 0.97 in group A (vs group B, $P = 0.085$ in the full analysis set, and $P = 0.028$ in the per-protocol set; vs group C, $P = 0.030$ in the full analysis set and $P = 0.020$ in the per-protocol set), -0.51 ± 0.65 in group B (vs group C, $P > 0.05$ in the full analysis set and the per-protocol set), and -0.36 ± 0.74 in group C. Decreases from baseline in body mass index, waist circumference and blood pressure were greater in group A than in group C.

Conclusion: With the provision of ready meals, the glycemic benefits of the investigational diet plan were demonstrable over a self-prepared food exchange system-based diet in Korean adults with established type 2 diabetes.

INTRODUCTION

It has been suggested that healthful eating patterns, rather than a specific composition of macronutrients, should be emphasized in medical nutrition therapy for diabetes¹. Several healthful eating patterns, such as the Mediterranean diet², the Dietary Approaches to Stop Hypertension (DASH) diet^{3,4} and plant-based diets⁵, have been suggested to promote health in people of various cultural backgrounds. However, most of these diets are difficult for people of East Asian cultural backgrounds to

follow, because wheat and rice are staple food sources in East Asian countries. Because some of the food items used in these recommended diets are not readily available or frequently used in local cuisine, lower acceptance of the Mediterranean and DASH diets is seen in East Asian people with diabetes.

Indeed, most previous randomized clinical trials (RCTs) that have examined the effects of the Mediterranean diet and the DASH diet on glycemic control in people with type 2 diabetes have been carried out in Western populations^{2,6,7}. The majority of study participants in these RCTs have been obese, limiting the extrapolation of results to non-obese East Asian

S-MJ and JA are the primary authors and contributed equally to this work.
Received 20 April 2020; revised 27 June 2020; accepted 12 July 2020

populations^{2,6,7}. To date, just a few cross-sectional studies have explored the benefits of the Mediterranean and DASH diets in Asian populations^{8,9}. These studies were not carried out in people with established type 2 diabetes, but rather in the general population, with primary study outcomes focusing on cardiometabolic risk factors rather than on glycemic outcomes.

To overcome the extremely high levels of carbohydrate consumption in East Asian countries, medical nutrition therapy for diabetes in East Asian countries usually relies on the use of a food exchange system¹⁰. Food exchange systems are considered outdated in most Western countries¹. East Asian people with type 2 diabetes tend to show less obesity than Western populations, and their saturated fat intake is already low. Thus, it is unclear whether a composition of low glycemic index, high dietary fiber content and/or high unsaturated fatty acid, which is absent in prevalent food exchange systems, can be beneficial in the diets of East Asian people with diabetes^{11–13}.

The purpose of the present RCT was to determine the glycemic benefits of an investigational diet plan comprised of substitute ingredients that mimic the average East Asian diet, but retain common characteristics of the Mediterranean and DASH diets^{2,6,7,14}, in adult Koreans with established type 2 diabetes. The substitute ingredients, and how to cook with them, were not as familiar to participants as the ingredients in conventional food exchange system-based diets¹⁰. For this reason, the investigational diet plan was prescribed for participants in the form of ready meals to minimize the possibility of poor compliance¹⁵. The benefits of the investigational diet plan were compared with benefits obtained with a food exchange system-based diet¹⁰ provided to two distinct groups either in the form of ready meals or not. This step was meant to examine whether benefits were obtained from the contents of the diet specifically, or from the provision of ready meals per se to adults with type 2 diabetes.

METHODS

The institutional review board of Samsung Medical Center approved the study protocol (SMC 2016-03-005-002), and written informed consent was obtained from all study participants.

Study design and participants

This was a 12-week, open-label RCT to compare the efficacy of three strategies of medical nutrition therapy for people with type 2 diabetes. The present study was carried out from 18 March 2016 to 17 February 2017 at the Samsung Medical Center in Seoul, Korea. This trial is registered with cris.nih.go.kr (number KCT0002217).

Physicians in the outpatient clinic invited adults aged 19–75 years with type 2 diabetes to participate in this trial according to criteria including a body mass index (BMI) of 18.5–30 kg/m², patients on a stable dosage of oral antihyperglycemic agents and with glycated hemoglobin (HbA1c) levels of 6.5–10.0%. Patients who opted to participate ($n = 63$) were screened for eligibility in detail on visit 1 (week –3 to –1), and

60 participants were randomized. Exclusion criteria included diagnosis of type 1 diabetes or gestational diabetes, use of exogenous insulin therapy, congestive heart failure and chronic kidney disease stage 4 or 5. Patient disposition, together with full inclusion and exclusion criteria, are available in Figure S1 and in the Supplemental Methods.

Procedures

Eligible participants were randomly assigned to groups including group A ($n = 20$), group B ($n = 20$) or group C ($n = 20$) at a 1:1:1 ratio following a simple randomization procedure without stratification, as detailed in the Supplementary Methods. All study participants in groups A, B and C received education on medical nutrition therapy for type 2 diabetes at day –1. In addition, the participants were informed of the characteristics of each diet plan, such as macronutrient distribution, food composition and expected eating patterns at the time of study entry. Because this education alone could not ensure that the participants would exactly follow the instructions, two pre-portioned ready meals per day (breakfast and dinner) were provided to participants in groups A and B by a metabolic kitchen (Dr. Kitchen Corp., Seoul, Korea) during the study period (12 weeks). The ready meals were previously prepared and cooked, so that participants would only need to heat them before consumption. Participants were instructed to plan the balance of their daily meals as instructed at the time of study entry. Calories were determined based on participants' ideal bodyweight and levels of physical activity using the Harris–Benedict formula. Calories per meal for a given ideal bodyweight were the same in groups A and B. The total daily energy intake except the ready meals, including self-prepared meals and snacks, of each participant in groups A and B was confirmed by a food diary.

In group A, the use of sugars and starches was restrained, whereas the amount of unsaturated fatty acid was increased to achieve a carbohydrate : fat : protein calorie ratio of 4:3:3, with net carbohydrates comprising 27% of total calories. Recipes in group A included meals comprised of substitute ingredients that mimic an average East Asian diet, as detailed in the Supplementary Methods. Of the total calorie intake, the proportion of saturated fat was ~4% and the proportion of unsaturated fat was ~15%. Among unsaturated fats, the proportions of monounsaturated fatty acids and polyunsaturated fatty acids were ~66% and ~34%, respectively. Sodium content was limited to 600–800 mg per meal to meet the goal of $\leq 2,300$ mg per day.

Recipes and ingredients used in meals for group B were based on the Food Exchange System in Korea¹⁰, with an average carbohydrate : fat : protein calorie ratio of 6:2:2, and with net carbohydrates and unsaturated fat comprising 48% and ~10% of total calories, respectively. Among unsaturated fats, the proportions of monounsaturated fatty acids and polyunsaturated fatty acids were ~64% and ~36%, respectively. The level of sodium content was the same as in group A.

In group C, participants were encouraged to follow the same guidelines used in group B, but no ready meals were supplied. Thus, participants had to prepare meals themselves.

Assessment

The primary end-point for the assessment of efficacy was the change in HbA1c from baseline to week 12. Secondary efficacy end-points included changes from baseline to week 12 in other important variables, including systolic and diastolic blood pressure, waist circumference, body composition, fasting blood glucose, proportion of participants with HbA1c <6.5% and ≥6.5%, proportion of participants with HbA1c <7.0% and ≥7.0%, fasting lipid parameters (total cholesterol, triglycerides, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol), and fasting insulin, homeostatic model assessment of insulin resistance and β-cell function (HOMA-IR and HOMA-β)¹⁶.

All adverse events (AEs) were recorded, and their severity and causal relationship to the provided meals were monitored. Details in the efficacy and safety assessments, and laboratory methods are described in the Supplemental Methods.

Statistical analysis

Efficacy analysis was carried out on the full analysis set (FAS), which included all participants for whom a post-baseline efficacy assessment was available, and on the per-protocol set (PPS), which included the subset of FAS participants who completed the study without any major protocol violations, including violations of inclusion and exclusion criteria. Analysis of the primary efficacy end-point was based on analysis of variance (ANOVA). Secondary end-points were analyzed in FAS and PPS participants. The significance of changes in secondary efficacy end-points among groups was evaluated by ANOVA.

Safety parameters were analyzed in the safety population set, which consisted of enrolled participants who received at least one dose of ready meals or self-prepared meals.

For sample size calculation, the null hypothesis was that the change in HbA1c from baseline to week 12 would not be different among the three groups. The expected difference in the change in HbA1c between groups B and C, and the expected difference in the change in HbA1c between groups A and C were both set to ≥0.5%¹⁵, a 5% significance level (α), 90% power (1- β) and 1:1:1 allocation to each group. The sample size was calculated as 20 participants per group (for a total of 60 subjects), as detailed in Supplementary Methods.

RESULTS

Among the eligible patients ($n = 60$), 53 had completed the study at week 12 (group A, $n = 16$; group B, $n = 20$; group C, $n = 17$; Figure S2). The mean daily total energy intake, excluding the ready meals, was 679.1 ± 76.7 kcal in group A and 639.7 ± 61.9 kcal in group B ($P = 0.2268$). Demographics and baseline characteristics were balanced among the groups (Table 1).

Changes in HbA1c (%) from baseline to week 6 were -0.84 ± 0.73 in group A (vs group B, $P = 0.021$ in FAS and PPS; vs group C, $P = 0.003$ in FAS and $P = 0.004$ in PPS), -0.39 ± 0.39 in group B (vs group C, $P = 0.270$ in FAS and PPS) and -0.23 ± 0.42 in group C (for FAS see Figure 1a–b and for PPS see Figure 3Sa–b). Changes in HbA1c (%) from baseline to week 12 were -0.97 ± 0.97 in group A (vs group B, $P = 0.089$ in FAS and $P = 0.028$ in PPS; vs group C, $P = 0.030$ in FAS and $P = 0.020$ in PPS), -0.51 ± 0.65 in group B (vs group C, $P = 0.563$ in FAS and PPS) and -0.36 ± 0.74 in group C (for FAS see Figure 1a,b, and for PPS see Figure 3Sa–b). A reduction from baseline in fasting plasma glucose (mg/dL) at week 6 was greater in PPS group A (-25.00 ± 43.65) than in group C (1.63 ± 19.14 , $P = 0.017$ in FAS and $P = 0.019$ in PPS; Figure S3c; data is not shown for FAS). Changes from baseline in HOMA-IR and HOMA-β at week 12 in FAS group A were not different from changes from baseline in HOMA-IR and HOMA-β at week 12 in groups B and C (Figure S4a,b; PPS data not shown). The change in high sensitivity C-reactive protein was significantly different between FAS groups B (-0.08 ± 0.27) and C (0.07 ± 0.23) at week 6 ($P = 0.033$), but there was no difference at week 12 (Figure S4c; PPS data not shown).

Reductions in low-density lipoprotein cholesterol, increases in high-density lipoprotein cholesterol and reductions in triglyceride in group A were significantly greater than in group C at week 12 among FAS participants (Figure S5a–d; PPS data not shown). Reductions in bodyweight (-1.70 ± 2.07 in group A vs 0.27 ± 1.13 in group C, $P < 0.001$), BMI (-0.68 ± 0.90 in group A vs 0.00 ± 0.48 in group C, $P = 0.010$; for FAS see Figure S4e and 4f; PPS data not shown), waist circumference (-1.70 ± 3.10 in group A vs 1.00 ± 3.01 in group C, $P = 0.008$; for FAS see Figure S5g; PPS data not shown), percentage total body fat mass (-1.36 ± 2.31 in group A vs 0.23 ± 1.90 in group C, $P = 0.023$) and percentage visceral fat (-0.01 ± 0.01 in group A vs 0.00 ± 0.01 in group C, $P = 0.014$; for FAS see Figure S5h–i; PPS data not shown) at week 12 were greater in group A than in group C. In the FAS participants with baseline BMI ≥23, weight reduction from baseline was significant in groups A (-2.38 ± 1.58 , $P = 0.001$; $n = 10$) and B (-1.67 ± 1.90 , $P = 0.015$; $n = 11$), but not significant in group C (-0.30 ± 1.15 , $P = 0.456$; $n = 9$). In the FAS participants with baseline BMI <23, weight reduction from baseline was not significant in any groups. Reductions in systolic (-1.90 ± 11.41 in group A vs 7.95 ± 11.92 in group C, $P = 0.011$) and diastolic blood pressure (-1.60 ± 7.96 in group A vs 5.00 ± 9.85 in group C, $P = 0.025$) between baseline and week 12 were greater in group A than in group C (for FAS see Figure S5j,k; PPS data not shown).

When paired *t*-tests were carried out for each group in FAS before and after the study period, there was a significant reduction from baseline in self-monitoring of blood glucose levels after breakfast (-59.7 ± 72.2 , $P = 0.011$) and before lunch (-29.6 ± 34.5 , $P = 0.001$) in group A, but not in groups B and C (Figure 2).

Table 1 | Demographics and baseline characteristics (full analysis set population)

	Group A (n = 20)	Group B (n = 20)	Group C (n = 20)
Age, years (range)	63.5 (51–75)	60.0 (44–74)	61.0 (34–74)
Male	9 (45%)	9 (45%)	13 (65%)
Weight (kg)	61.4 (50.0–76.6)	61.8 (52.0–78.0)	62.5 (48.7–79.5)
BMI (kg/m ²)	23.5 ± 2.1	23.7 ± 1.8	23.3 ± 1.85
Waist circumference	84.05 ± 6.49	83.90 ± 6.56	82.95 ± 4.70
Percent total body fat mass	26.08 ± 6.98	26.86 ± 6.36	24.05 ± 5.59
Proportion of visceral fat	0.90 ± 0.04	0.90 ± 0.04	0.89 ± 0.04
Years since diabetes diagnosis	15.0 (6–26)	13.0 (2–30)	14.0 (1–24)
HbA1c (%)	7.77 ± 0.91	7.70 ± 0.67	7.74 ± 0.96
Fasting insulin (mU/L)	9.23 ± 7.08	14.07 ± 12.93	7.90 ± 4.66
HOMA-IR	3.54 ± 2.80	5.10 ± 4.48	2.91 ± 1.77
HOMA-β	42.44 ± 37.41	65.78 ± 70.34	37.12 ± 27.20
Oral antihyperglycemic agents			
No. medications			
Monotherapy	4 (20%)	4 (20%)	6 (30%)
Met	4 (20%)	3 (15%)	6 (30%)
Dual therapy	8 (40%)	9 (45%)	8 (40%)
Met + DPP4i	6 (30%)	2 (10%)	3 (15%)
Met + SU	1 (5%)	4 (20%)	4 (20%)
Triple therapy	8 (40%)	7 (35%)	6 (30%)
Met + DPP4i + SU	6 (30%)	3 (15%)	4 (20%)
Type of medication			
Met	20 (100%)	16 (80%)	19 (95%)
DPP4i	13 (65%)	7 (35%)	9 (45%)
SU	8 (40%)	12 (60%)	11 (55%)
SGLT2i	2 (10%)	4 (20%)	1 (5%)
TZD	0	1 (5%)	0
AGI	1 (5%)	3 (15%)	0
Lipid-modifying drugs	13 (65%)	14 (70%)	15 (75%)
Statins	13 (65%)	14 (70%)	14 (70%)
Ezetimibe	1 (5%)	1 (5%)	1 (5%)
Omega-3 acid ethylester	0	2 (10%)	0
Antihypertensive therapy	9 (45%)	5 (25%)	8 (40%)
ACEI	1 (5%)	2 (10%)	1 (5%)
ARB	8 (40%)	3 (15%)	7 (35%)
Aspirin	7 (35%)	5 (25%)	7 (35%)
Microvascular complications			
Diabetic retinopathy	3	2	4
Diabetic kidney diseases			
Microalbuminuria	0	1	1
Decreased eGFR [†]	4	2	1
Diabetic polyneuropathy	3	3	0

Data are expressed as medians (range), Data presented as *n* (%), or mean ± standard deviation. [†]All had an estimated glomerular filtration rate (eGFR) of 45–60 mL/min per 1.73 m². ACEI, angiotensin-converting enzyme inhibitor; AGI, alpha-glucosidase inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; DPP4i, dipeptidyl polypeptide-4 inhibitor; eGFR, estimated glomerular filtration rate; FAS, full analysis set; HbA1c, glycosylated hemoglobin; HOMA, homeostatic model assessment; IR, insulin resistance; Met, metformin; SGLT2i, sodium–glucose cotransporter 2 inhibitor; SU, sulfonylurea; TZD, thiazolidinedione.

Among the safety population set (*n* = 60), four patients in group A and one patient in group B reported one or more AEs, without significant differences between groups. Three patients in group A and one patient in group B reported one or more events of hypoglycemia. Another AE

that developed in group A was “dyspepsia.” Otherwise, all AEs were judged unrelated to dietary interventions, and did not cause discontinuation of the investigational diet. There were no serious AEs, and all of the AEs were classified as “mild.”

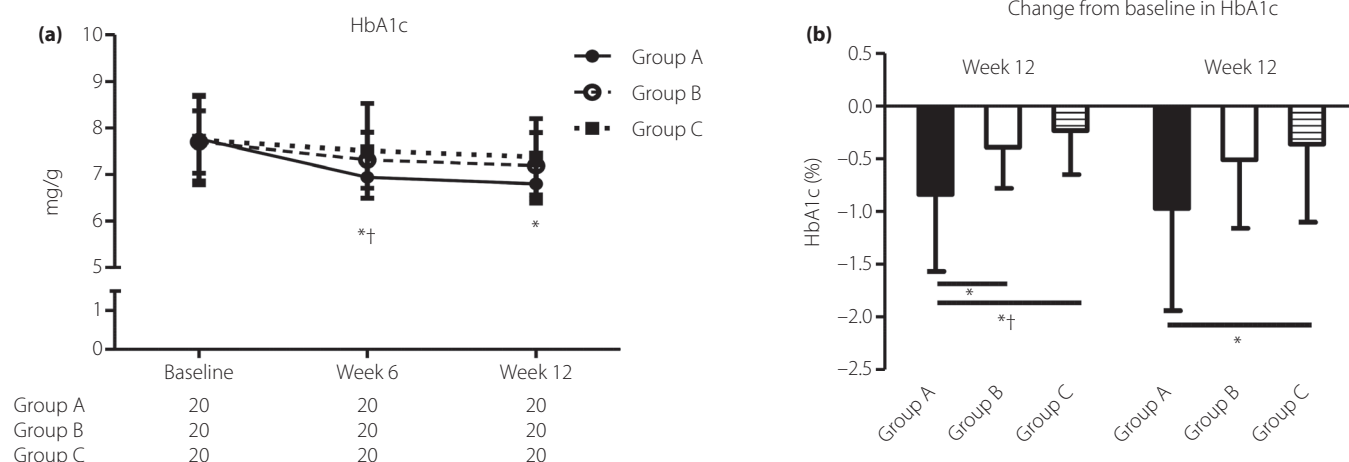


Figure 1 | Glycemic outcomes during the study period in the full analysis set participants. (a) Glycated hemoglobin (HbA1c). (b) Change from baseline in HbA1c. *Group A versus group B, $P < 0.05$; †group A versus group C, $P < 0.05$.

According to the satisfaction section of the questionnaire, the mean proportion of meals for which study participants described their levels of satisfaction as “very satisfied,” “okay” and “not satisfied” with regard to taste was not different between groups A and B (Figure S6).

DISCUSSION

In the present RCT, the glycemic benefits of the investigational diet plan provided in the form of ready meals (group A) were demonstrable in comparison with the benefits of a food exchange system-based diet prepared by the participants (group C) in intention-to-treat analysis. Given the significant difference in the primary outcome between groups A and B was observed only in PPS, but not in FAS, it is likely that the benefits of the investigational diet plan were obtained by the combined effects from the specific contents of the diet and the provision of ready meals to the participants. This difference manifested as early as week 6, consistent with the findings of previous studies examining the effects of the DASH diet⁷ and the Mediterranean diet¹⁷. Among the three groups, only group A showed markedly reduced post-breakfast and pre-lunch glucose levels on 7-point self-monitoring of blood glucose on day 85. Key differentiators in designing diets for groups A and B in the present study were a reduction in the amount of net carbohydrates (sugars and starches), the use of ingredients with a lower glycemic index, an increase in dietary fiber content and an increase in unsaturated fatty acid intake in group A relative to group B. All of these factors were likely to have had profound effects on reducing postprandial glucose excursions in participants with type 2 diabetes.

Although a simple low-carbohydrate diet for people with type 2 diabetes has been shown to be effective in terms of glucose lowering, as well as reduction of cardiovascular risk factors in the short term, the benefit over diet plans with

higher carbohydrate contents has not been shown in a meta-analysis involving long-term studies¹⁸. A recent meta-analysis¹⁹ reported a significant benefit of a low-carbohydrate diet for type 2 diabetes patients, in terms of HbA1c at 1 year. In that meta-analysis, however, the significance mostly depended on a large-scale study evaluating effects of a Mediterranean-style diet², rather than studies of a simple low-carbohydrate diet. No studies, except this single study, included in the meta-analysis showed a significant benefit of low-carbohydrate diet in terms of HbA1c at one year¹⁹. In fact, several long-term studies showed that diet plans with relatively high carbohydrate, but with low glycemic index and high fiber, contents result in favorable results. Given that drastic changes in carbohydrate contents would make a diet plan harder to follow in the longer term, we chose to use the Mediterranean and DASH diets, which involve more moderate reduction of carbohydrate, but also encourage the intake of unsaturated over saturated fatty acid.

Several RCTs carried out among obese people with type 2 diabetes have explored the glycemic benefits of the Mediterranean diet^{2,17}, the DASH diet^{7,14} and vegetarian diets⁶. However, just a few of these RCTs designate glycemic control as the primary outcome^{2,6,7}. The diet used in group A in the present study was closer to the Mediterranean^{2,17} or DASH diet^{7,14} than to a vegetarian diet⁶ in terms of carbohydrates and unsaturated fat contents. It is notable that glycemic benefits were reproducible from the findings of previous studies in obese participants, even though the median BMI was 23.5 kg/m² among participants in the current study. In addition, the investigational diet plan (group A) also showed significant reductions in BMI, bodyweight and blood pressure measures in participants in comparison with the group C diet. These findings are consistent with the findings of previous studies carried out with obese participants with type 2 diabetes^{2,6,7}.

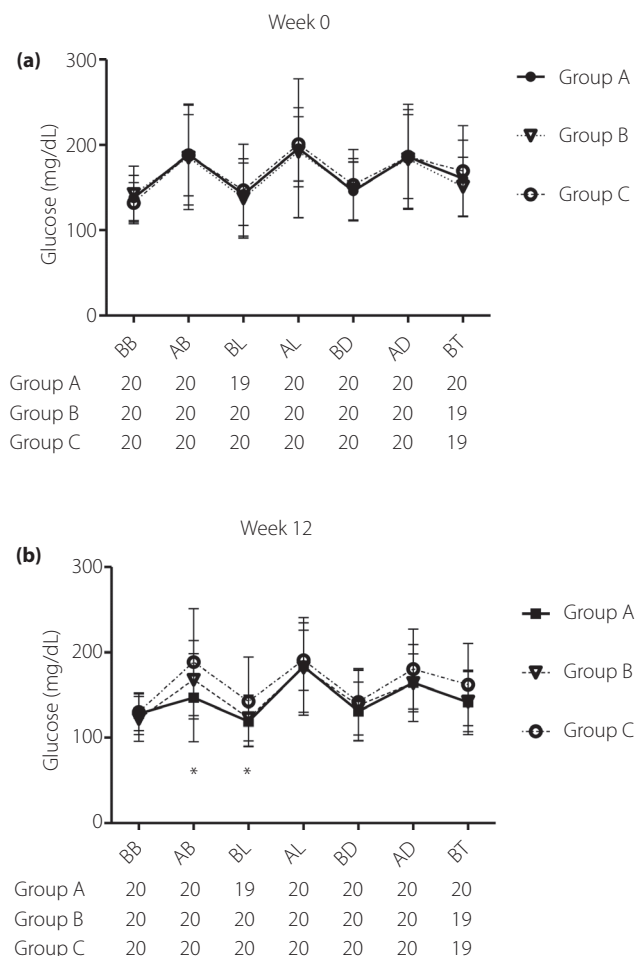


Figure 2 | Seven-point self-monitored blood glucose profiles (a) before and (b) after the study period at day 85 in the full analysis set participants. In each group, the values from the same participants before and after the study period were compared by paired *t*-tests. Note that 23% of the ready meals in group A, and 14% of the ready meals in group B were taken as lunch instead of dinner, although the ready meals were originally provided as breakfast and dinner. *Before versus after the study period in group A, *P* < 0.05. AB, after breakfast; AD, after dinner; AL, after lunch; BB, before breakfast; BD, before dinner; BL, before lunch; BT, bedtime.

Two randomized clinical trials with Japanese people with type 2 diabetes compared the efficacy and safety of the low-carbohydrate diet and calorie-restricted diet. Although there was no calorie restriction in the low-carbohydrate diet groups in both studies, the total calorie intake achieved during the study period was not different between the low-carbohydrate diet and calorie-restricted diet groups in the Yamada *et al.* study²⁰, and was lower in the low-carbohydrate diet group in the Sato *et al.* study²¹. Although self-monitoring of blood glucose profiles were not presented in both studies, greater reduction in HbA1c was demonstrable in both studies. Loss of bodyweight, achieved by

lower calorie intake, was not a requisite for the benefit of a low-carbohydrate diet in the Yamada *et al.* study²⁰ and a previous study carried out in a Western population²².

Several new aspects distinguish the present study from previous RCTs that used the Mediterranean and DASH diets in obese Western populations. First, this study provides direct RCT evidence in an East Asian population based on East Asian food culture. A profound decrease in postprandial glucose levels was shown to be achievable in the East Asian study population, where postprandial hyperglycemia is more profound and obesity is less common than in Western populations. Glycemic benefits were not shown to be associated with decreased patient satisfaction in terms of taste, which stands to promote the use of substitute ingredients compatible with the East Asian food culture. Second, the present study utilized two control groups (one with and one without the provision of ready meals) to differentiate the relative contributions of dietary contents and delivery method to overall positive outcomes.

We recognize several limitations of this study. Importantly, the primary outcome was significantly different between groups A and B in PPS, but not in FPS. Because the difference in the primary outcome between the groups A and B in PPS might be due to attrition bias or small sample bias, it should be noted that it is inconclusive whether the benefit in the primary outcome was from dietary contents or delivery method. In this context, it should also be noted that the total calorie intake in group C was not confirmed by a food diary, although the total energy intake was similar between groups A and B. Subgroup analysis of the participants with BMI ≥ 23.0 kg/m² also showed that significant weight reduction from baseline was observed only in the participants in groups A and B, but not in group C. Therefore, it is uncertain whether the difference between groups A and C in intention-to-treat analysis was from the dietary composition, or from the combined effect of dietary composition and energy intake. In addition, the study period was insufficient to document the long-term benefits of the tested dietary patterns. In this regard, further long-term studies, possibly consisting of a ready meals phase, a transition phase and maintenance phases with minimal provision of ready meals¹⁵, might extend the clinical implications herein.

In conclusion, the present study provides RCT-supported evidence of the glycemic benefits of a diet plan, provided to participants in the form of ready meals, comprised of substitute ingredients that mimic the average East Asian diet, but still retain common characteristics of the Mediterranean and DASH diets, for Korean adults with established type 2 diabetes having a median BMI of 23.5 kg/m². The significant benefit might be attributable to the combined effects from the specific contents of the diet and the provision of ready meals to the participants.

ACKNOWLEDGMENTS

This study was supported by Dr. Kitchen Corp., Seoul, Korea.

DISCLOSURE

The authors declare no conflict of interest.

REFERENCES

- American Diabetes A. 4. Lifestyle management: standards of medical care in diabetes-2018. *Diabetes Care* 2018; 41: S38–S50.
- Esposito K, Maiorino MI, Ciotola M, *et al.* Effects of a Mediterranean-style diet on the need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes: a randomized trial. *Ann Intern Med* 2009; 151: 306–314.
- Cespedes EM, Hu FB, Tinker L, *et al.* Multiple healthful dietary patterns and type 2 diabetes in the women's health initiative. *Am J Epidemiol* 2016; 183: 622–633.
- Ley SH, Hamdy O, Mohan V, *et al.* Prevention and management of type 2 diabetes: dietary components and nutritional strategies. *Lancet* 2014; 383: 1999–2007.
- Rinaldi S, Campbell EE, Fournier J, *et al.* A comprehensive review of the literature supporting recommendations from the Canadian diabetes association for the use of a plant-based diet for management of type 2 diabetes. *Can J Diabetes* 2016; 40: 471–477.
- Barnard ND, Cohen J, Jenkins DJ, *et al.* A low-fat vegan diet and a conventional diabetes diet in the treatment of type 2 diabetes: a randomized, controlled, 74-wk clinical trial. *Am J Clin Nutr* 2009; 89: 1588S–1596S.
- Azadbakht L, Fard NR, Karimi M, *et al.* Effects of the Dietary Approaches to Stop Hypertension (DASH) eating plan on cardiovascular risks among type 2 diabetic patients: a randomized crossover clinical trial. *Diabetes Care* 2011; 34: 55–57.
- Kim Y, Je Y. A modified Mediterranean diet score is inversely associated with metabolic syndrome in Korean adults. *Eur J Clin Nutr* 2018; 72: 1682–1689.
- Tiong XT, Nursara Shahirah A, Pun VC, *et al.* The association of the dietary approach to stop hypertension (DASH) diet with blood pressure, glucose and lipid profiles in Malaysian and Philippines populations. *Nutr Metab Cardiovasc Dis* 2018; 28: 856–863.
- Paik HY, Lee HK. Korean food exchange system. *Diabetes Res Clin Pract* 1990; 9: 103–107.
- Dehghan M, Mente A, Zhang X, *et al.* Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. *Lancet* 2017; 390: 2050–2062.
- Ha K, Kim K, Chun OK, *et al.* Differential association of dietary carbohydrate intake with metabolic syndrome in the US and Korean adults: data from the 2007–2012 NHANES and KNHANES. *Eur J Clin Nutr* 2018; 72: 848–860.
- Won JC, Lee JH, Kim JH, *et al.* Diabetes fact sheet in Korea, 2016: an appraisal of current status. *Diabetes Metab J* 2018; 42: 415–424.
- Azadbakht L, Surkan PJ, Esmailzadeh A, *et al.* The dietary approaches to stop hypertension eating plan affects C-reactive protein, coagulation abnormalities, and hepatic function tests among type 2 diabetic patients. *J Nutr* 2011; 141: 1083–1088.
- Rock CL, Flatt SW, Pakiz B, *et al.* Weight loss, glycemic control, and cardiovascular disease risk factors in response to differential diet composition in a weight loss program in type 2 diabetes: a randomized controlled trial. *Diabetes Care* 2014; 37: 1573–1580.
- Jin SM, Choi SH, Choi DW, *et al.* Glucagon/insulin ratio in preoperative screening before pancreatic surgery: correlation with hemoglobin A1C in subjects with and without pancreatic cancer. *Endocrine* 2014; 47: 493–499.
- Shai I, Schwarzfuchs D, Henkin Y, *et al.* Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *N Engl J Med* 2008; 359: 229–241.
- Dyson P. Low carbohydrate diets and type 2 diabetes: What is the latest evidence? *Diabetes Ther* 2015; 6: 411–424.
- Huntriss R, Campbell M, Bedwell C. The interpretation and effect of a low-carbohydrate diet in the management of type 2 diabetes: a systematic review and meta-analysis of randomised controlled trials. *Eur J Clin Nutr* 2018; 72: 311–325.
- Yamada Y, Uchida J, Izumi H, *et al.* A non-calorie-restricted low-carbohydrate diet is effective as an alternative therapy for patients with type 2 diabetes. *Intern Med* 2014; 53: 13–19.
- Sato J, Kanazawa A, Makita S, *et al.* A randomized controlled trial of 130 g/day low-carbohydrate diet in type 2 diabetes with poor glycemic control. *Clin Nutr* 2017; 36: 992–1000.
- Nuttall FQ, Gannon MC. Metabolic response of people with type 2 diabetes to a high protein diet. *Nutr Metab (Lond)* 2004; 1: 6.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1 | Examples of ready meals.

Figure S2 | Patient disposition.

Figure S3 | (a) Glycated hemoglobin and change from baseline in (b) glycated hemoglobin (HbA1c) and (c) fasting plasma glucose in the per-protocol set (PPS).

Figure S4 | (a) Homeostatic model assessment of β -cell function (HOMA- β), (b) homeostatic model assessment of insulin resistance (HOMA- R) and (c) high sensitivity C-reactive protein (hs-CRP) in the full analysis set (FAS).

Figure S5 | Lipid parameters, bodyweight, body mass index and blood pressure during the study period in the full analysis set (FAS) participants.

Figure S6 | The taste satisfaction during the study period in groups A and B.