# Effect of pre-meal consumption of protein-enriched, dietary fiber-fortified cereal bar on long-term glycemic control in patients with type 2 diabetes

Trial No: NCT03727854

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1. Aim of this study

The aim of this study is to evaluate the effect of premeal protein-enriched bar in long-term glycemic control in patients with type 2 diabetes mellitus. Glucose levels in subjects who intake premeal protein-enriched bar with dietary modification will be compared to those in subjects who only do the dietary modification.

2. Methods

1> Inclusion/Exclusion criteria

1) Inclusion criteria

• BMI 18.5~35 kg/m2

• Type 2 diabetes patients

• Fasting blood glucose ≥ 126 mg/dl or

• HbA1c ≥ 6.5% or • Subjects who were previously diagnosed with type 2 diabetes and who have been treated with lifestyle modification only, oral anti-diabetic drugs or basal insulin.

2) Exclusion criteria

- HbA1c < 6.5% or > 10%
- Subjects using insulin other than basal insulin
- Subjects who have newly started or have changed anti diabetic drugs within 3 months
- Subjects who are allergic to grains, nuts, legumes and milk
- Previous history of gastrointestinal surgery (except for hemorrhoid surgery, appendectomy surgery and hernia surgery)
- Subjects with chronic unstable disease
- Subjects with cognitive inpairment who are not able to follow the study protocol
- Females who are pregnant or doing breast feeding
- Subjects with Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) levels of higher than 3 times of upper normal ranges
- Subjects with hemoglobin level of less than 10.0 g/dL

• Subjects with alcohol addiction or drug abuse

2> Detail methods

This study was conducted as a randomized, open-labeled study (Figure 1). The study subjects first assessed whether they met the criteria for selection and exclusion on the 0th visit day, and then enrolled in the study. They individually received diet education and were required to do self-monitoring of blood glucose seven times a day [7-point SMBG] until the next visit. Only those who have visited on the first visit day passed the screening test, and performed the 7-point SMBG correctly, were registered for the study. Subjects enrolled in the study were randomly assigned to pre-meal protein enriched bar with dietary modification group or dietary modification only group. After the 12 weeks, the second visit and study-end exam was conducted.

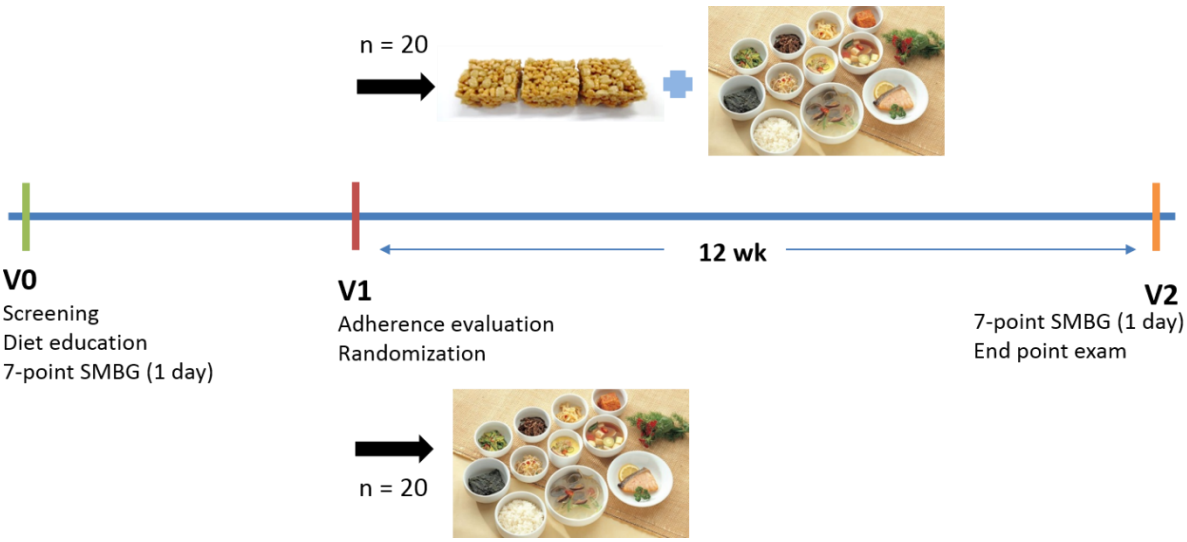


**Figure 1. An overview of the study**

1) Signing the consent to participate in the study and confirming for the inclusion and exclusion criteria (Visit 0, screening visit)

-Those willing to participate in the study visited the Seoul National University Hospital Clinical Trial Center with 12 hours of fasting.

-It was confirmed that the person who signed the agreement satisfies the criteria for inclusion and exclusion of study subjects. Blood tests were performed and medical history surveys, anthropometric measurements (height, weight, abdominal circumference) were done. Blood tests include complete blood count, fasting plasma glucose, hemoglobin A1c,

aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum creatinine, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, Insulin, and C -peptide.

-After conducting the above test, the study subjects were individually provided with diabetes dietary education.

-7-point SMBG (before / after each meal, before bedtime) should be conducted for one day to evaluate compliance.

-If the criteria for inclusion and exclusion are satisfied and all 7-point SMBG for one day has been performed, the subject is selected as the final study.

-If 7-point SMBG is not performed, revisit after one week and write 7-point SMBG again.

2) Study start (1st visit date)

-The study subjects visited the clinical trial center of the Seoul National University Hospital until the appointed time on the first visit day.

-After randomization, in a pre-meal protein-enriched bar with a dietary modification group, the cereal bar is consumed 15 minutes before meals and required to follow the diet education. In the control group, they are required to follow diet education without a pre-meal cereal bar.

-A single intake of protein-enriched cereal bar is 36 g, and its calories are 97 kcal and consists of 16.5 g of carbohydrate (12.2 g of dietary fiber), 12.5 g of protein, and 0.6 g of fat.

-A protein-enriched cereal bar is recommended to consume three times a day (at least two times a day is mandatory)

-It is recommended that both groups maintain physical activity according to their usual exercise habits during the study period.

-In order to maintain compliance, the research nurse calls the research subjects every four weeks after the start of the study to check whether they are good at maintaining the diet and protein-enriched cereal bar as instructed and encouraging them to increase compliance.

-During the last week (week 11), subject subjects should conduct a 7-point SMBG on a day that is possible.

-Subjects should not change their existing diabetes medications and doses during the

study period.

3) Rescue strategy

- In the SMBG result, if the blood glucose level is more than 270 mg / dL at week 0-6, or more than 240 mg / dL at week 7-12 for three consecutive days, subjects were required to contact the clinical trial center to determine whether a visit is necessary. For those who do not use anti-diabetes drugs, lifestyle modification should be strengthened, or the use of oral anti-diabetes medications should be started. For those who were using only oral anti-diabetes medications, the drug dose should be increased, or another drug added. For those who were using basal insulin, they are required to increase the insulin dose.

-If the subject experience more than one hypoglycemia (less than 70 mg/dL), they are required to contact the clinical trial center to determine if a visit is necessary. Re-evaluation of the underlying disease should be performed in the case of subjects who have not previously used anti-diabetes medications, and in the case of subjects who have used oral anti-diabetes drugs, the existing drugs should be reduced or discontinued. Those who have been using basal insulin, the insulin dose should be reduced.

4) Outcome measurement

-Subjects visited the clinical trial center at 12 weeks ± 1 week of study. At the time of visit, fasting blood glucose sampling and body measurements were performed while fasting was maintained for 12 hours.

-As the primary end point, change in HbA1c from baseline was evaluated.

-Secondary endpoints include fasting blood glucose, body weight, weight circumference, blood lipid levels (triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol), HOMA-IR, HOMA-beta.

5) Statistical analysis

Descriptive statistics are expressed as mean ± standard deviation (SD) for continuous variables, and categorical variables are expressed as number and percentage. For comparison of baseline characteristics between the intervention group and the control group, t-test (when the normal distribution is satisfied) and Mann-Whitney U test (when the normal

distribution is not satisfied) are used for continuous variables and Pearson's chi-square test for categorical variables. To evaluate the difference between the 12th week and the baseline data, the paired t-test or Wilcoxon's signed-rank test was used for the continuous variables, and the McNemar's test was used for the categorical variables. The primary and secondary endpoints were evaluated using ANCOVA methods. All statistical analysis was performed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism 5 (GraphPad Software Inc., San Diego, CA, USA). If the P-value is less than 0.05, it is evaluated as statistically significant.