Impact of Meal Timing on Postprandial Interstitial Fluid Glucose Levels in Young Japanese Females

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Summary Flash glucose monitoring (FGM) provides continuous and accessible measurement of the interstitial fluid glucose (ISFG) level and this system is useful for understanding blood glucose fluctuations. We examined differences in postprandial ISFG after the main mealtimes (breakfast, lunch, and dinner) in healthy young Japanese females. Nine healthy young females (aged 21.5±0.6 y old) were enrolled in this study. ISFG was continuously measured by FGM. Participants ate the same meal three times a day consecutively, thereby satisfying their daily energy requirements. Postprandial ISFG fluctuations were evaluated for 4 h after each meal. There were no significant differences in ISFG before the 3 main meals. The postprandial ISFG peak was the lowest after breakfast, increasing in the order of lunch and then dinner. The area under the curve of the 4-h postprandial ISFG was higher after lunch and dinner than after breakfast. The results of this study suggest that postprandial ISFG differ depending on mealtimes in young Japanese females.

Key Words flash glucose monitoring, identical meal condition, mealtime, glucose fluctuation, healthy individuals

High glucose spikes after a meal, but not changes in fasting glucose, are associated with a high risk of obesity, metabolic syndrome, and type 2 diabetes mellitus (1, 2). Several studies have shown that postprandial blood glucose fluctuations differ minimally among breakfast, lunch, and dinner in healthy participants (3, 4). To date, catheterization and multiple blood samplings have been required to investigate 24-h blood glucose fluctuations, but such testing is burdensome for participants. In recent years, continuous glucose monitoring (CGM) and flash glucose monitoring (FGM) systems have been used as substitutes for the painful fingertip blood glucose test required for self-management of diabetes. Zhou et al. investigated 24-h interstitial fluid glucose (ISFG) levels in healthy Chinese participants by CGM and reported postprandial ISFG levels after breakfast to be lower than those after lunch and dinner (5). However, previous studies have not clarified daily trends in postprandial glucose fluctuations with mealtimes, because the calories consumed at breakfast were set lower than those at lunch and dinner (5). In this study, the content and proportion of meals contribute to postprandial hyperglycemia (6, 7). Therefore, differences in postprandial glucose levels at each mealtime should be investigated while maintaining identical meal contents.

In this pilot study, we examined the effects of postprandial ISFG, with maintenance of equal meal contents, in healthy young Japanese females.

Participants and Methods

Participants. Nine healthy females 21–23 y of age (mean age 21.5±0.6 y, BMI 20.7±1.5 kg/m²) were recruited for this study. Sample size of this pilot study was calculated to provide a statistical power of 80% and a difference in peak postprandial ISFG of 30 mg/dL between breakfast and dinner (6). This study was approved by the ethics committee of the University of Shizuoka (approval number: 1-53) and followed the Declaration of Helsinki and Ethical Guidelines for Medical and Health Research Involving Human Subjects. The study was registered in the UMIN Clinical Trials Registry (ID: UMIN000039932).

Study design. Participants received an explanation of the objectives and details of the study and consented to participate. The protocol of this study is presented in Fig. 1. FGM (FreeStyle Libre Pro, Abbott Japan Co., Ltd., Matsudo, Japan) sensors were precisely attached to the participants according to the manufacturer’s instructions and ISFG was monitored for 10 d. ISFG was measured automatically every 15 min. The first trial started from breakfast 2 d after FGM attachment. The daily energy requirements of each participant were calculated to provide a statistical power of 80% and a difference in peak postprandial ISFG of 30 mg/dL between breakfast and dinner (6). This study was approved by the ethics committee of the University of Shizuoka (approval number: 1-53) and followed the Declaration of Helsinki and Ethical Guidelines for Medical and Health Research Involving Human Subjects. The study was registered in the UMIN Clinical Trials Registry (ID: UMIN000039932).

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Contents, four consecutive times during the trial. They started to consume the test meals at 7:30 am, 12:30 pm, 18:30 pm, and 7:30 am the next day and completed them within 15 to 20 min. The postprandial ISFG levels after the first breakfast were excluded from the data analysis to remove the influences of the previous diet. Intake between meals was limited to water. The participants rested for 30 min before eating the test meals. After eating the test meals, all participants had to stay at the trial site for 4 h. There were no constraints on daily activities of participants during the trial period except for intense exercise. The same test was performed on day 9 and the FGM sensors were then removed on day 10 at noon.

Statistical analysis. We calculated the area under the curve (AUC) using ISFG from 0 to 240 min after the start of eating, by applying the trapezoid rule to assess postprandial changes in ISFG. The trial was performed again 5 d later and AUC at the times of each meal were averaged. The data are shown as means ± SD. Statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) using the Friedman test with post hoc Bonferroni correction for non-parametric variables.

Results and Discussion

The postprandial ISFG results are shown in Fig. 2. The results of similar tendency were shown in two trials. Before the meal was eaten, baseline ISFG levels did not differ significantly among the mealtimes (mean value of breakfast: 71 ± 9 mg/dL, lunch: 78 ± 10 mg/dL, and dinner: 75 ± 10 mg/dL). However, the peak ISFG value after breakfast was significantly lower than those after lunch and dinner and that after dinner was the highest (mean value of breakfast: 118 ± 13 mg/dL, lunch: 137 ± 13 mg/dL, and dinner: 155 ± 21 mg/dL; p < 0.05). The delta-AUC (ΔAUC) of ISFG was significantly increased at lunch and at dinner as compared with that at breakfast. Furthermore, the ΔAUC of ISFG at dinner was significantly higher than that at lunch (Fig. 3).

The results of this study show postprandial ISFG fluctuations at breakfast to be significantly diminished as compared to those at lunch and dinner in young Japanese females. Previous studies have shown that large meals (50% of total daily energy) at dinner increase postprandial blood glucose levels more than similarly-size meals at breakfast (6). In this study, similar results were confirmed even though our test meal size (33% of total daily energy) was equalized among the meal times. The results suggest the postprandial blood glucose levels after breakfast to be less affected by meal size than that after dinner, actually showing the opposite phenomenon. In obese women with metabolic syndrome, a lifestyle characterized by consumption of a high-energy breakfast and low-energy dinner decreases body weight and improves insulin sensitivity more than a low-energy breakfast and high-energy dinner, even under conditions of identical caloric intake in a single day (8). In addition, a high-energy diet at dinner increases the risk of obesity and type 2 diabetes. The content and size of a meal are both important for assuring a healthy meal, but the time of day that the meal is consumed may also merit consideration. The results of our present study confirm that the dietary pattern of reducing energy intake at dinner reduces postprandial ISFG fluctuations and thereby promotes reduction of the risks of obesity and diabetes.

Many young females are extremely concerned about body weight and shape and tend to strive to lose weight. False perceptions of body weight and shape can lead to dietary problems associated with excessive weight loss, such as skipping meals and consuming an unbalanced diet (9, 10). Ogata et al. reported that repeatedly skip-
Meal timing might cause abnormal glucose fluctuations (11). Since unhealthy lifestyles in young individuals increase the risks of obesity and lifestyle-related diseases after middle age (12, 13), understanding the pattern of postprandial glucose fluctuations might be useful when considering dietary habits.

In conclusion, this study is the first to examine the effects of mealtime on fluctuations in ISFG levels by using FGM. We showed that the peak of ISFG levels was lowest after breakfast, followed by lunch and finally dinner. The interval to return to baseline ISFG after lunch and dinner took longer than after breakfast. Different hormonal response or sensitivity at each meal timing like insulin or incretin hormones (14, 15) might explain our finding. We hope that these results will be useful as a reference for establishing healthy dietary habits of young Japanese females.

**Authorship**

RT and TY designed the research; RT, TY, HT, and NO performed the research and interpretation of data; TY and TH were involved in gaining ethical approval; TY and TH wrote the first draft of the manuscript; and all authors reviewed and edited the manuscript and approved the final version of the manuscript.

**Disclosure of COI**

The authors have no conflicts of interest, financial or otherwise, to disclose.
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