Divided consumption of late-night-dinner improves glycemic excursions in patients with type 2 diabetes: A randomized cross-over clinical trial

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Aims: To explore the acute effect of late-night-dinner and divided dinner on postprandial glucose levels in patients with type 2 diabetes.

Methods: Sixteen patients were randomly assigned to this cross-over study. Each patient wore a continuous glucose monitor for 5 days and consumed identical test meals for 3 days. Patients consumed the test meals of dinner at 2100 h (D21) or divided dinner (vegetable and rice at 1800 h and the vegetable and the main dish at 2100 h) on the second or fourth day, and dinner at 1800 h (D18) on the third day. The daily glucose parameters were compared within-patient for 3 days.

Results: D21 demonstrated significantly higher values of incremental area under the curve (IAUC) for glucose 2300 to 0800 h (644 ± 156 vs. 147 ± 63 mmol/L C21 h, p < 0.01, mean ± standard error of the mean) and incremental glucose peak (IGP) after dinner (6.78 ± 0.79 vs. 3.09 ± 0.62 mmol/L, p < 0.01) compared to those of D18. Moreover, the mean amplitude of glycemic excursion (MAGE) of D21 tended to be higher than that of D18 (6.99 ± 0.60 vs. 5.35 ± 0.51 mmol/L, p = 0.077). However, the divided dinner significantly reduced IAUC 2300 to 0800 h (142 ± 60 mmol/L C21 h, p < 0.01), IGP after dinner (3.75 ± 0.58 mmol/L, p < 0.01), and MAGE (5.33 ± 0.41 mmol/L, p < 0.01) compared to those of D21.

Conclusion: Our findings demonstrated that consuming late-night-dinner led to postprandial hyperglycemia, and this postprandial hyperglycemia can be ameliorated by consuming a divided dinner.

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Postprandial hyperglycemia plays a major role in micro and macrovascular complications in patients with type 2 diabetes [1–5], and reducing postprandial hyperglycemia is thus an important goal for patients with type 2 diabetes. Postprandial glucose levels are influenced by meal size, the amount of carbohydrates [6,7], the macronutrient composition [8], intestinal absorption [9], hormone secretion, gastric emptying [10,11], and food order [12,13]. Unhealthy habits such as skipping breakfast and late-night eating have been shown to be associated with weight gain and obesity [14–17]. However, the effect of the late-night-dinner on postprandial glucose levels has not been extensively studied in patients with type 2 diabetes.

We hypothesized that late-night-dinners would increase postprandial glucose levels in patients with type 2 diabetes. Therefore, in this randomized controlled, a within-patient, cross-over study, we assessed the effect of the late-night-dinner on the postprandial glucose levels in patients with type 2 diabetes.

2. Methods

2.1. Patients

Interested patients were initially screened and informed of study requirements from the outpatient at Kajiyama Clinic, Kyoto, Japan. The period of recruitment and the study period was from September 2014 to April 2015. We included the patients with type 2 diabetes who did not work a night shift within the last 2 years and who did not cross time zones within the last 6 months of this study. Patients were excluded in cases of steroid use, insulin treatment, impaired renal or liver function, diabetic retinopathy, and cardiovascular diseases. The patients habitually woke up between 0600 h and 0800 h and went to sleep between 2200 h and 0800 h. The study protocol was conformed to the 1975 Declaration of Helsinki and was approved by the Ethics Committee of Osaka Prefecture University and Kyoto Women’s University, and was registered at Clinical Trials gov. (UMIN 000015108). All patients gave written informed consent to participate in the study and for the study’s findings to be published.

2.2. Study design

This was a randomized, open-label, cross-over, within-patient clinical trial. Two weeks prior to the study, the patients underwent an examination to obtain their anthropometric measurements with blood sampling for fasting plasma glucose, and for HbA1c after an overnight fast. The patients’ characteristics such as medical history and current medication use were also recorded.

During the test period, each patient wore a continuous glucose monitor (CGM, iPro2, Medtronic Japan, Tokyo) for 5 days and consumed identical test meals for 3 consecutive days from the second to the fourth day (Fig. 1). On the first day, each patient arrived at the clinic at 1600 h, and the patient was fitted with a CGM by a clinic nurse. The patients were also provided a self-monitoring blood glucose device (SMBG, Sanwa Kagaku Kenkyusyo, Aichi, Japan) and were instructed to perform the required sensor calibration procedure four times daily. Each patient consumed the identical test meals of breakfast at 0800 h, lunch at 1300 h, and dinner at 2100 h or a divided dinner (tomato and rice at 1800 h, and the spinach and the main dish at 2100 h) on the second or the fourth day, and dinner at 1800 h on the third day at home.

According to the randomized cross-over design, the patients were assigned by dietitians at the clinic wherein they consumed either the divided dinner or the dinner at 2100 h on the second or fourth day. During the study period, the patients were instructed 24-h food record and a 24-h 4 to 5-point SMBG profile (pre-breakfast, lunch, dinner and bedtime readings). Compliance was explained by the face to face meeting individually before and the first day of the study and reinforced with a phone call during the study period by the dietitians of the clinic. On the fifth day, patients returned to the clinic at 1100 h, the CGM was removed, and its data were uploaded and stored electronically.

The daily glucose parameters were compared within-patient for the 3 days of the consumption of the identical dinner at different times. The mean plasma glucose and standard deviation glucose were calculated from 0800 to 0800 h in the next morning. The incremental area under the curves (IAUC) for glucose of 2300–0800 h were calculated by the trapezoidal method above the baseline value for glucose at 1800 h. The incremental glucose peaks (IGPs) were calculated as the maximal blood glucose excursion from the fasting value over the 5-h postprandial period. The mean amplitude of glycemic excursions (MAGE) were calculated from 0800 h to 0800 h in the next morning as described [18].

2.3. Test meals

Patients consumed an identical breakfast, lunch, and dinner by the test meals for 3 days during the test periods at home (Table 1). The test meals, which consisted of boiled white rice, white bread, milk, vegetable, and frozen lunch boxes of gluten-meat steak and fried fish with vegetable (Tokatsu Foods, Yokohama, Japan), had the same macronutrient content and composition within-patient in 3 study days. The composition and nutritional content of the test meals were analyzed by computer software (Microsoft Excel Eiyokun for Windows Ver.7.0, Kenpakusya, Tokyo). The test meals were adjusted to meet the caloric requirement of each patient, calculated by 27 kcal/kg/day, by adjusting the amount of carbohydrate with the mean of a sample population prescribed a 1570 kcal per day. The frozen lunch boxes of gluten-meat steak and fried fish with vegetable were provided by the research group, and rice, bread, milk, and other vegetable were prepared by the patients according to the study broche made for each patient by the dietitians. Each patient was indicated to measure all food precisely and record the amount and time of every meal. The patients consumed the first dish of vegetables for 5 min, then the main dish for 5 min, and rice/bread for 5 min in their entirety within 15 min each test meal time. The records of food amount, meal time, and blood glucose values obtained by SMBG of each patient were col-
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