Original Article

Eating glutinous brown rice for one day improves glycemic control in Japanese patients with type 2 diabetes assessed by continuous glucose monitoring

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Background and Objectives*:* We investigated whether intake of non-glutinous brown rice (BR) or glutinous brown rice (GBR) for 1 day had an influence on the daily glucose profile measured by continuous glucose monitoring (CGM) when compared with intake of non-glutinous white rice (WR). **Methods and Study Design***:* A total of 37 inpatients with type 2 diabetes mellitus (T2DM) were recruited for a 3-day randomized triple cross-over trial in which they ate WR, BR, or GBR for 1 day each. One of the three types of rice was eaten at breakfast, lunch, and dinner on the first day, before switching to the other types on the second and third days. Each meal had the same energy content and the same side dishes. The main outcome measures were the blood glucose profile determined by continuous glucose monitoring (CGM) and the profile of serum C-peptide (CPR) for 3 hours after breakfast. A self-administered questionnaire was used to assess the palatability of each type of rice. **Results***:* According to the CGM data, the mean 24-hour glucose concentration was lowest with GBR ($p<0.01$). Serum C-peptide showed no significant differences among the three diets. Regarding palatability, BR was assigned significantly lower scores than WR and GBR ($p<0.05$), while there was no difference between WR and GBR. **Conclusions***:* GBR intake suppressed the whole-day glucose profile of patients with T2DM, mainly by reducing postprandial glucose excursion, and GBR was preferred over BR with respect to palatability. GBR may be worth adding to the diet of patients with T2DM.

Key Words: type 2 diabetes, diet, continuous glucose monitoring, glutinous brown rice, postprandial hyperglycemia

INTRODUCTION

The objectives of treating type 2 diabetes mellitus (T2DM) are to maintain or improve the quality of life and to prevent the development of diabetic complications through good glycemic control. To achieve these objectives, lifestyle modification (diet and exercise) is essential with or without pharmacotherapy. Regarding diet, most patients are instructed to obtain 50-60% of their total energy requirement from carbohydrates.[1] In the Asian region, rice is a major source of carbohydrates, and Japanese tend to prefer white rice to brown rice with respect to taste and palatability. However, white rice contains less dietary fiber and trace elements (such as K, Mg, or Mn) than brown rice because these are mainly found in the bran, which influences insulin secretion and/or insulin sensitivity.[2] Thus, intake of white rice may be disadvantageous for prevention or treatment of diabetes when compared with brown rice.

A recent cohort study of 60,000 Japanese persons demonstrated that the risk of T2DM increases along with the increase in the intake of white rice.[3] The authors suggested that white rice with its lower content of dietary fiber is rapidly absorbed from the intestine, leading to postprandial hyperglycemia that may be associated with a higher incidence of diabetes. Conversely, Aune et al reported that replacement of refined grains, including rice and other cereals, with whole grains may reduce the risk of T2DM based on a meta-analysis of 16 prospective cohort studies.[4] Similarly, the epidemiological analysis of Hu et al showed that the risk of T2DM could be reduced by 16% if daily intake of 50 g of white rice was replaced with brown rice having the same energy content.[5] Thus, the usefulness of brown rice or whole grain cereal for prevention of T2DM has been suggested by epidemiological studies, but the direct effect of these grains on the glucose profile has not been fully investigated. Accordingly, it is important to evaluate the effect of brown rice on postprandial glucose excursion compared with white rice in T2DM patients.

Japanese tend to prefer white rice over brown rice because brown rice is drier due to inclusion of bran. Rice

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can be classified into glutinous and non-glutinous types. In Japan, the former type is mainly used in rice cakes, while the latter is generally boiled and eaten with daily meals. The starch in glutinous rice is 100% amylopectin, while non-glutinous rice has starch consisting of 80% amylopectin and 20% amylose, and the stickiness of glutinous rice is based on this difference in the composition of starch. Because glutinous brown rice is not drier and tastes good despite containing bran, a frozen boiled glutinous brown rice product is already being marketed commercially in Japan. In the present study, we aimed to verify whether intake of non-glutinous brown rice (BR) or glutinous brown rice (GBR) for one day could improve the daily glucose profile measured by continuous glucose monitoring (CGM) compared with that after intake of non-glutinous white rice (WR). In addition, we compared the taste and texture of BR and GBR with WR by performing a questionnaire survey.

MATERIALS AND METHODS

Participants

Thirty-seven Japanese patients with T2DM were recruited from the inpatient diabetes unit of St. Marianna University Hospital (Kawasaki, Japan). They had been admitted for treatment of diabetes, and fasting blood glucose was maintained at <140 mg/dL by diet with or without oral hypoglycemic agents and/or insulin. Patients with cancer, anemia, renal failure, chronic liver disease, thyroid disease, or pregnancy were excluded. Physical activity was not restricted, but was voluntarily limited by the subjects to quiet activities (such as reading or watching television). This study was conducted in accordance with the ethical principles of the Declaration of Helsinki, and was approved by the ethics committee of St. Marianna University School of Medicine (No. 2242). All patients gave written informed consent prior to participation.

Dietary intervention

The study was performed according to a cross-over and counterbalanced design involving six possible orders of treatment. Patients were studied on three consecutive days; they ate WR, BR, or GBR on 1 day each, while the other dishes of each meal were unchanged throughout the study. They were randomly allocated to six groups, depending on the order of eating the three types of rice [WR on the first day, BR on the second day, and GBR on the third day (WR/BR/GBR), WR/GBR/BR, BR/WR/GBR, BR/GBR/WR, GBR/WR/BR, and GBR/BR/WR]. Test meals were eaten three times a day (breakfast, lunch, and dinner), and each meal consisted of a staple food (WR, BR, or GBR) and side dishes. Patients selected their preference from among 4 side dishes (omelet, hamburger, white fish fillet, or salmon) for breakfast, lunch, or dinner. After selecting a side dish, the patient ate the same dish at the same meal every day for three days, and only the staple food was changed. The total energy and nutrition intake was equivalent for all types of meal (26.5±1.7 kcal/kg of ideal body weight). There were no subjects who had previously been eating brown rice on a daily basis.

Clinical measurements

Anthropometric measurements such as height and weight were obtained for all participants using standardized techniques, and BMI was calculated. Venous blood samples were collected at 0, 30, 60, 120, and 180 min after breakfast for measurement of plasma glucose, serum C-peptide, and plasma lipids [triglycerides (TG), total cholesterol (TC), and free fatty acids (FFA)]. The plasma glucose concentration was measured by the hexokinase UV method and serum C-peptide was determined by the CLEIA method. Plasma lipids were determined by enzymatic methods. Results were expressed as the mean±standard deviation (M±SD).

CGM protocol

Continuous glucose monitoring (CGM) system (iProTM2; Medtronic, Northridge CA, USA) was used to measure subcutaneous interstitial glucose concentrations on an ambulatory basis for 72 consecutive hours. The sensor was inserted on day 0 and was removed in the mid-morning on day 4. All of the patients also performed self-measurement of blood glucose (SMBG) at least 4 times daily using a blood glucose monitor (OneTouch Ultra; Life scan, Milpitas, CA, USA), and input the data into the CGM recorder for calibration. They were instructed to calibrate the system at least 2 h after meals. The average glucose value was recorded every 5 mins, resulting in 288 measurements in 24 h. To evaluate the effect of the type of rice on daily glucose excursion, CGM data obtained from the start of breakfast to just before breakfast on the next morning were used to calculate the 24 hour mean glucose concentration, its standard deviation (SD), and the mean amplitude of glucose excursion. In addition, the incremental area under the glucose curve for 3 hours ($IAUC\text{-}G_{3h}$) after the start of each meal was calculated at breakfast, lunch, and dinner on each day. Results were expressed as the mean±SD.

Food palatability questionnaire

To assess the palatability of WR, BR, and GBR, a self-administered questionnaire was completed after dinner on each day. The questionnaire consisted of the following five items: taste (delicious or not), texture (rice cake-like or dry), consumability (can be eaten every day or not), habitual intake (possible to consume for one meal every day or not), and satiety (feeling of fullness or not). Each item was assigned a score, which could range from the most positive response (+3 points) to the most negative response (-3 points).

Statistical analysis

Results were expressed as the mean±SD. One-way ANOVA followed by a multiple comparison test (Bonferroni's method) was used to compare the effects of WR, BR, and GBR. All analyses were performed using Excel-Toukei 2012 (Social Survey Research Information Co., Ltd.). Differences were considered to be significant if the probability value (p) was less than 0.05.

RESULTS

Characteristics of the subjects

Among the 37 subjects registered in the present study, 7

Table 1. Subjects characteristics

Characteristic	
n (men/women)	17/13
Age (years)	61.1±12.5
BMI (kg/m^2)	26.3±3.9
Obese (BMI ≥25 kg/m^2), [% (n)]	73.3 (22)
HbA1c (%)	8.7±1.4
Fasting serum C-peptide (ng/mL)	1.4±0.9
Diabetes treatment, [% (n)]	
Diet	16.7 (5)
Oral hypoglycemic agent	13.3 (4)
Insulin (plus oral hypoglycemic agent)	66.7 (20)
Glucagon like peptide-1 receptor agonist (including oral hypoglycemic agent)	3.3 (1)

Data are the mean±SD or n.

were excluded from analysis because they required emergency treatment (n=2) or because of insufficient glucose data due to CGM problems (n=5). Table 1 displays the clinical characteristic of the remaining 30 subjects. The baseline age was 61.1±12.5 years, BMI was 26.3±3.9 kg/m^2, HbA1c was 8.7±1.4% and fasting C-peptide was 0.4±0.9 ng/mL. Regarding the treatment of diabetes, 5 patients were on diet alone, 4 were also taking oral medications, 20 were also using insulin, and 1 subject was also taking lixisenatide (a glucagon like peptide-1 receptor agonist).

Plasma glucose and serum CPR in the first 180 minutes after breakfast

After breakfast, the area under the plasma glucose concentration vs. time curve (AUC-PG) and the AUC of serum C-peptide (AUC-CP) were not significantly different among the three types of rice (9036±6254 [(mg/dL)·min] and 437±347 [(mg/dL)·min], respectively, with WR; 8897±6113 and 348±269, respectively, with BR; and 7317±5596 and 456±626, respectively, with GBR). The concentrations of plasma lipids (TG, TC, and FFA) also showed no significant differences among the 3 types of rice after breakfast.

Circadian variation of blood glucose detected by CGM

Figure 1A displays the whole-day glucose profile when the patients ate each type of rice as determined by CGM. As shown in Figure 1B, the 24-hour mean glucose concentration was significantly lower when the patients ate GBR (126.3±22.0 mg/dL) than when they ate WR (144.2±28.5), while there was no significant difference from WR with BR (137.2±29.8). However, there were no significant differences of the 24-hour glucose SD and mean amplitude of glucose excursion among the three types of rice (35.6±14.6 mg/dL and 58.0±21.3 mg/dL, respectively, with WR; 37.6±15.9 and 61.6±23.5, respectively, with BR; and 33.2±13.2 and 57.1±21.5, respectively, with GBR). As shown in Table 2, the IAUC-G$_{3h}$ after lunch and the total IAUC-G$_{3h}$ across three meals were significantly lower with GBR than WR, but there were no significant differences for these parameters between BR and WR (25391±6824 [(mg/dL)·min] and 83812±17601 [(mg/dL)·min], respectively, with GBR; 29418±9430 and 90373±24121, respectively, with BR; and 30740±7262 and 93306±21427, respectively, with WR). We also assessed the glucose profile according to each treatment and found it to be similar regardless of the treatment group (Supplemental figure 1).

Palatability of the 3 types of rice

The results of the questionnaire for the 3 types of rice are shown in Figure 2 (taste, texture, consumability, habitual intake, and satiety). The total score of BR was significantly lower than those of WR and GBR (3.4±5.3 for BR, 6.5±5.9 for WR, and 6.7±3.6 for GBR; p<0.05), while there was no significant difference between WR and GBR. Regarding the individual items, BR received significantly lower scores for taste and texture than GBR (p<0.05 and p<0.01, respectively), and BR also received a significantly lower consumability score than WR (p<0.05).

DISCUSSION

There were three main findings of the present study. First, the AUC-PG and AUC-CP over 3 hours after the start of breakfast showed no significant differences following intake of the three types of rice. Second, the 24-hour mean glucose concentration and the total IAUC-G$_{3h}$ across three meals were significantly lower with GBR than WR, while there were no significant differences between BR and WR. Third, the palatability of GBR was similar to that of WR.

In this study, the effect of GBR could not be detected by intermittent measurement of plasma glucose after breakfast, but was revealed by detailed assessment of the whole-day glucose profile using CGM. While BR did not improve glucose excursion compared with WR in the present study and its palatability was inferior to that of WR, intake of GBR ameliorated both postprandial and whole-day glucose excursion (Figure 1A). In addition, the subjects considered that the palatability of GBR was better than that of BR and similar to WR. Previous studies have demonstrated that increasing dietary fiber intake improves glycemic control due to suppression of the peak postprandial blood glucose concentration.[6,7] Mohan et al compared the effect of WR, BR, and BR with legumes on

Table 2. Three-hours postprandial AUC with each type of rice

		WR	BR	GBR	p value
Breakfast	(mg/dL) · min	31645±8000	31446±8996	29465±6277	0.073
Lunch	(mg/dL) · min	30740±7262	29418±9430	25391±6824**	0.000
Dinner	(mg/dL) · min	30921±8639	29508±8981	28956±7890	0.208
Total	(mg/dL) · min	93306±21427	90373±24121	83812±17601**	0.001

WR: white rice; BR: brown rice, GBR: glutinous brown rice.
Data are the mean±SD
Difference vs WR according to multiple comparison by Bonferroni's test **; p<0.01.

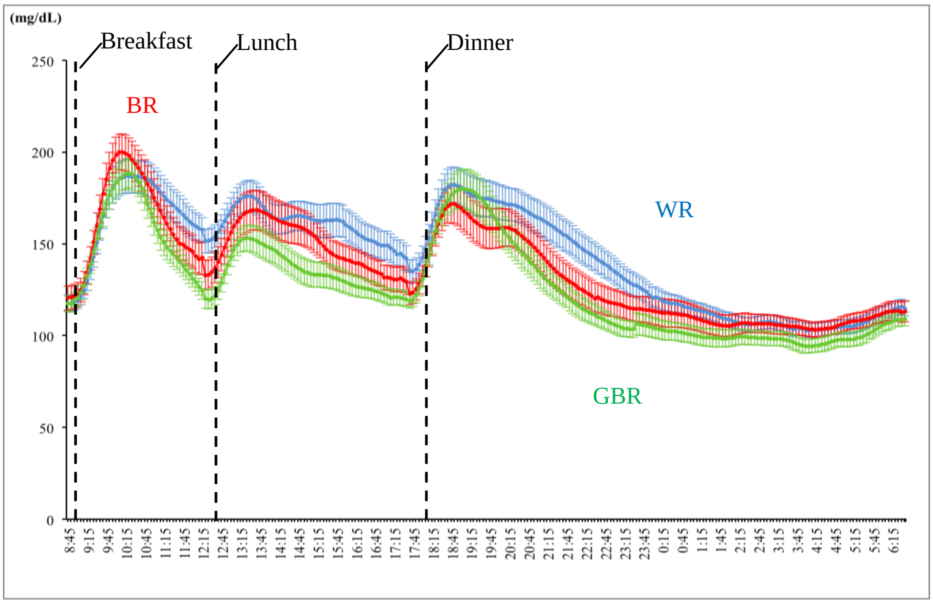

Figure 1A. Average glucose concentration profile over 24 hours determined by continuous glucose monitoring in patients with T2DM fed white rice (WR), brown rice (BR), or glutinous brown rice (GBR). Data are expressed as the mean±SD (N=30). Dotted lines show the start glucose of eating breakfast, lunch, and dinner.

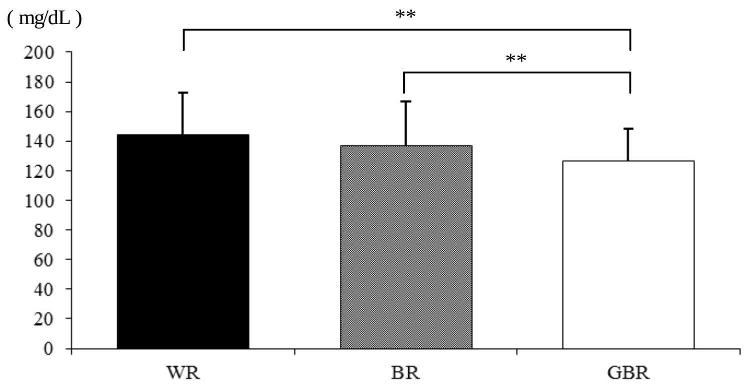

Figure 1B. Comparison of the 24-hour mean glucose concentration determined by continuous monitoring in patients with T2DM fed white rice (WR), brown rice (BR), or glutinous brown rice (GBR). Data are expressed as the mean±SD (N=30). ***p*<0.01 by multiple comparison with Bonferroni's test.

postprandial glucose.[8] Their subjects who ate BR and BR with legumes groups, which are rich in dietary fiber, had lower peak postprandial glucose concentrations compared with those who ate WR. In the present study, the average daily intake of dietary fiber was 12.7 g with the WR meal, 22.0 g with the BR meal, and 23.3 g with the GBR meal, so dietary fiber intake was much higher with BR and GBR. However, the increment of glucose from just before a meal to the postprandial peak was similar among the 3 meal types when assessed by CGM (Figure 1A). On the other hand, the postprandial decline of glucose from peak to trough was largest with GBR. Thus, the mechanism underlying postprandial suppression of glucose concentrations by GBR was unrelated to dietary fiber. Since intake of refined glutinous rice has been reported to increase postprandial glucose concentrations compared with WR,[9] the difference of starch between glutinous and non-glutinous rice also fails to explain the glucose-lowering effect of GBR.

We measured intrinsic insulin secretion in the morning after breakfast and found no difference of AUC-CP among the three types of rice, but we did not assess whole-day insulin secretion. Accordingly, the precise effect of GBR or BR on insulin secretion compared with WR is not clear. Regarding this issue, Shimabukuro et al reported that intake of BR for 8 weeks improved HOMA-IR and reduced visceral fat in subjects with metabolic syndrome.[10] In addition, Weickert et al found that even short-term intake of a fiber-rich cereal diet for only 3 days could improve insulin resistance as assessed by euglycemic-hyperinsulinemic clamp.[11] However, the effect of GBR on insulin sensitivity has not been evaluated before. The bran of BR is enriched in trace elements, vitamins, and polyphenols, and some of the components of bran (such as K, Mg, Mn, and thiamine) are known to influence insulin secretion or insulin sensitivity.[2,12] We did not analyze the bran of BR and GBR in this study, but comparison of these brans and evaluation of their effect on insulin secretion/insulin sensitivity needs to be done in the future to provide clues to the mechanism underlying the effect of GBR.

To precisely assess the palatability of each type of rice,

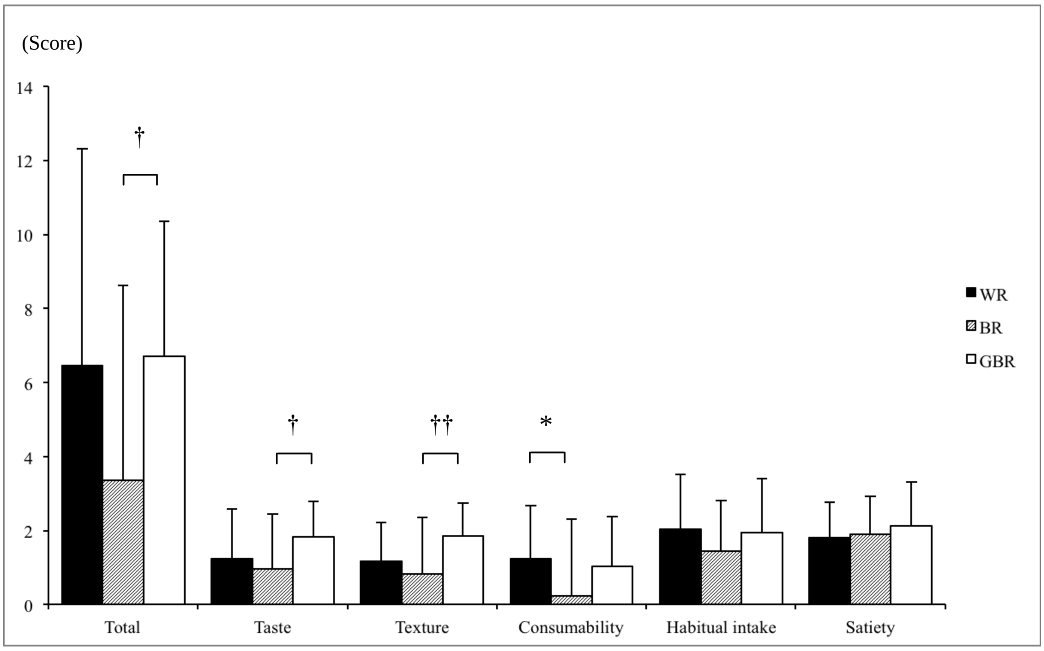

Figure 2. Palatability of white rice (WR), brown rice (BR), and glutinous brown rice (GBR) results of a questionnaire covering 5 items (taste, texture, habitual intake, consumability, and satiety) using a bipolar 7-point ordinal scale ranging from -3 to +3. The scores for each item and the total score are shown. Data are expressed as the mean±SD (N=30). *$p<0.05$ vs WR and $^{\dagger}p<0.05$, $^{\dagger\dagger}p<0.01$ vs GBR by multiple comparison with Bonferroni's test.

a blinded design would have been desirable, but we employed an open label cross-over design in the present study because of the difficulty of blinding the different types of rice. Accordingly, we could not exclude the possibility of bias, and lack of familiarity with the taste or texture of GBR might also have influenced the palatability scores assigned by the patients. On the other hand, the habitual intake and satiety scores were similar among the three types of rice. There were striking differences of taste, texture, and consumability between BR and GBR in spite of their similar appearance. Thus, GBR appeared to overcome the problem of poor palatability associated with BR.

There were some limitations of the present study. First, the number of patients was small and the study period was only one day for each meal. Second, the whole-day glucose profile was determined by CGM rather than by blood sampling. Third, we did not assess either insulin sensitivity or whole-day intrinsic insulin secretion. Thus, further research into the mechanism underlying the effect of GBR and a longer clinical study in a larger patient population are required for confirmation of our findings.

In conclusion, one-day intake of GBR suppressed the whole-day glucose profile in patients with T2DM, mainly by modifying postprandial glucose excursion, and GBR was preferred over BR with respect to palatability. It may be worth adding GBR to the diet of patients with T2DM.

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AUTHOR DISCLOSURES
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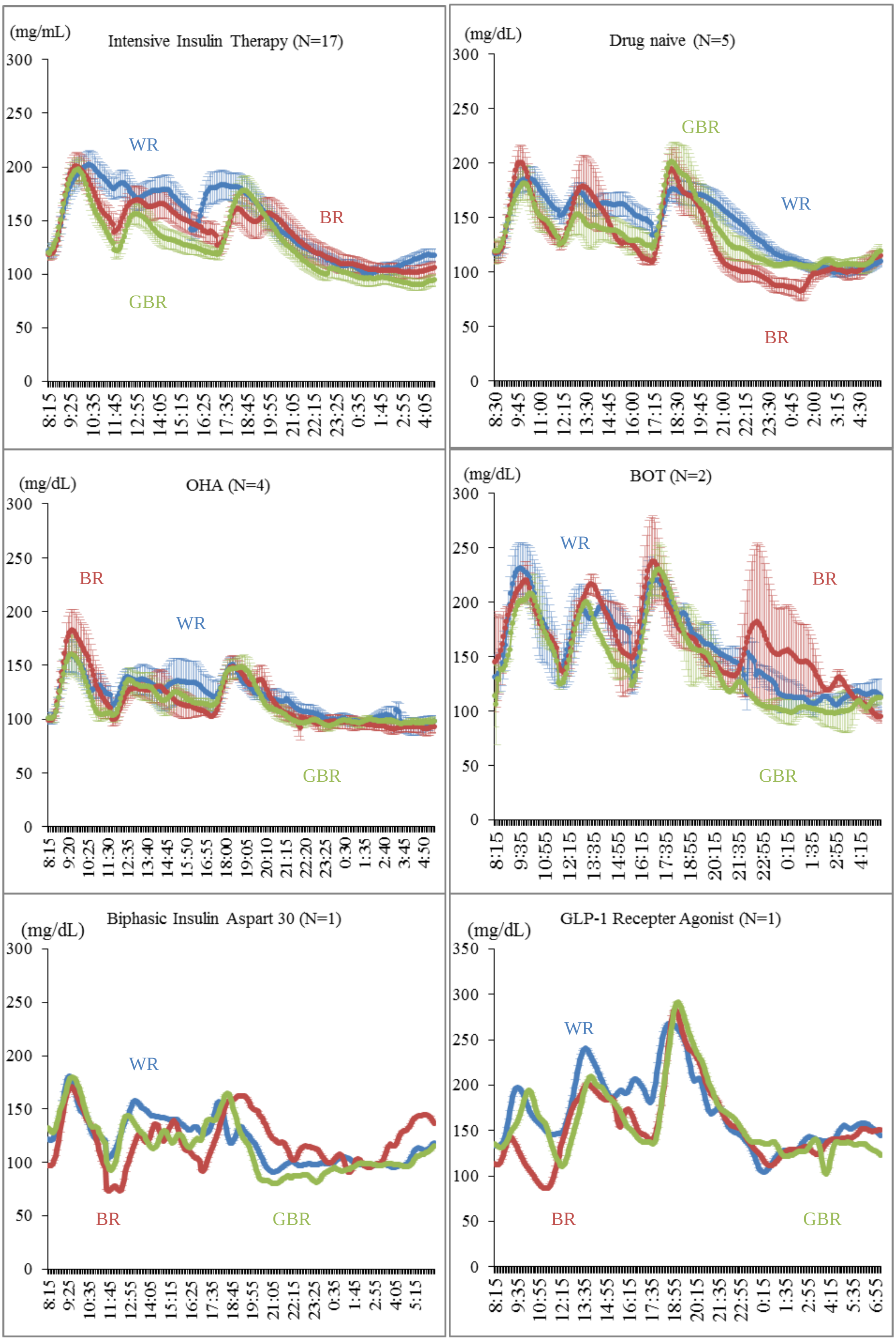

Supplemental figure 1: Average glucose concentration profile over 24 hours determined by continuous glucose monitoring in patients with T2DM treated with intensive insulin treatment (N=17), drug naïve (N=5), oral hypoglycemic agents only (N=4), basal supported oral therapt (N=2), or GLP-1 receptor agonist (N=1), biphasic insulin aspart 30/70 (N=1).