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Effect of High β-glucan Barley on Postprandial Blood Glucose Levels in Subjects with Normal Glucose Tolerance: Assessment by Meal Tolerance Test and Continuous Glucose Monitoring System

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ABSTRACT

The effect of white rice (WR) mixed with high β-glucan-containing barley at 50% on improvement of postprandial blood glucose levels was assessed by meal tolerance test and continuous glucose monitoring (CGM) in 15 healthy subjects with normal glucose tolerance (age 31.6 ± 12.9 years old, 4 males and 11 females). A meal tolerance test (500 kcal) was conducted using 2 types of test meals: a test meal only with WR and a test meal WR mixed 50% barley, and the side dish was the same in both meals. Blood glucose levels of the subjects 180 minutes after ingestion of the test meals were compared. In addition, a CGM device was attached to the subjects for 2 days when the WR or barley as a staple food was provided 3 times a day for consecutive days, and the daily variation of glucose was investigated. The glucose levels 30 minutes after dietary loads and the area under the blood concentration-time curve over 180 minutes were significantly decreased in the barley consumption group. In CGM, 24-hour mean blood glucose and 24-hour standard deviation of blood glucose were also significantly decreased after ingestion of the barley. Postprandial glucose level elevation was suppressed by mixing high-β-glucan barley with WR in subjects with normal glucose tolerance.

Keywords: Diet therapy; Beta glucan; Barley; Postprandial hyperglycemia; Glucose monitoring; Meal tolerance

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INTRODUCTION

The prevalence of overweight and obesity is increasing world-wide and the disease burden related to high body mass index (BMI) has increased [1]. In Japan, obesity and glucose intolerance are increasing as well [2]. Health hazards and mortality related to obesity and overweight are increasing, and it is believed to be possible to suppress the onset of heart disease, type 2 diabetes and cancer by appropriately controlling weight [3-5]. It is well known

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Conflict of Interest

The authors declare that they have no competing interests.

that postprandial hyperglycemia causes insulin resistance, and is a risk factor for obesity and cardiovascular diseases [6,7]. The amount of carbohydrate contributes most to the increase in postprandial blood glucose [8-10], and it is said that even if it is the same carbohydrate, blood glucose elevation may vary depending on the quality [11]. Glycemic index (GI) is an indicator of carbohydrate quality which ranks carbohydrates based on the rate of the glycemic response [11]. It is reported that brown rice and barley have a lower GI value and a suppressive effect on postprandial blood glucose elevation, because they contain a larger amount of dietary fiber than white rice (WR) [12-14]. Barley contains a lot of insoluble and water-soluble dietary fiber, and most of the water-soluble dietary fiber is β-glucan [15,16]. It has been pointed out that β-glucan may reduce the risk of cardiovascular diseases through its blood cholesterol-lowering action and other effects [17]. There is growing evidence that postprandial generation of both oxidative stress and inflammation are one important mechanism for the initiation and progression of endothelial dysfunction in type 2 diabetes [7], but it is not clear whether subjects with normal glucose tolerance show similar results.

Asians have traditionally consumed WR as a staple food which is said to constitute a healthy diet, however, it is a high GI food [9]. High intake of WR can causes an increase in the postprandial blood glucose and is known to be associated with an increased risk of diabetes and metabolic syndrome [18]. In a previous study, it is reported that the intake of high β-glucan barley led to reduction of visceral fat [19], however, no detailed report regarding blood glucose levels has been published. If the postprandial blood glucose can be lowered by mixing barley with WR to lower GI, this will be an effective way for preventing diabetes or obesity.

We conducted meal tolerance tests using test meal of WR mixed with 2-rowed hull-less barley which contains a higher content of β-glucan (7.2 g per 100 g) than commonly consumed barley [20] in subjects with normal glucose tolerance and examined whether high-β-glucan barley improves postprandial blood glucose or not. In addition, continuous glucose monitoring (CGM) was used to assess daily variation of blood glucose.

MATERIALS AND METHODS

Study subjects

We recruited the subjects who were normal in a 75 g oral glucose tolerance test, not taking any medications and their hemoglobin A1c (HbA1c) was 5.5% or less in Saiseikai Yokohamashi Tobu Hospital. Fifteen subjects (4 males and 11 females) with normal glucose tolerance were chosen after explaining the purpose of this study. The age of the subjects was 31.6 ± 12.9 years. The mean BMI, fasting glucose and HbA1c were 20.3 ± 5.6 kg/m^2, 90.3 ± 8.1 mg/dL, 5.0% ± 0.2%, respectively. The study was conducted according to the guidelines of the Declaration of Helsinki and all procedures were approved by the Ethics Committee of the Saiseikai Yokohamashi Tobu Hospital (approval number 2013030). Written informed consent was obtained from all subjects.

Meal tolerance test

The subjects fasted after 21:00 on the day before the test and ingested test meals adjusted to approximately 500 kcal in the early morning. The meal tolerance test was conducted for 2 consecutive days. Two types of diets were prepared: one consisted of only WR as staple food and a side dish (WR diet), and the other consisted of WR mixed with 50% β-glucan rich barley (BR) as staple food and the same side dish as WR diet (BR diet). The barley used in this study

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is "Kirarimochi," which was registered as a new breed of 2-rowed hull-less barley in 2009 and contains a high amount of β-glucan (7.2 g per 100 g) [20]. It was developed by the National Agriculture and Food Research Organization in Japan. The β-glucan content of normal covered barleys is about 4%, whereas Kirarimoch has β-glucan content of 5.8%. This barley line is not a genetically modified crop. The high-β-glucan barley was pearled to remove the bran (pearled to 60% yield) and the remaining 60% was used as rice-shaped barley [20]. The BR diet consisted of 50% high-β-glucan rice-shaped barley (Kirarimochi) and 50% rice. The test meals were ingested for about 15 minutes. This study was conducted by cross-over design and the subjects were divided into 2 groups. The meal of the first day was assigned WR or BR in turn. Each group was assigned either WR or BR diet on the first day and switched to the other type on the following day in turn. The WR diet contained 504 kcal, 80 g of carbohydrate (glucose 76.9 g and dietary fiber 3.5 g), 18.7 g protein, and 11.4 g lipid, while the BR diet contained 479 kcal, 75 gcarbohydrate (glucose 68.8 g and dietary fiber 6.3 g), 18.9 g protein, and 11.6 g lipid. The amount of the staple food was adjusted to 150 g for both the WR and BR diets.

Blood glucose was measured before, 30, 60, 120, and 180 minutes after ingestion of each diets. Plasma triglyceride and free fatty acid (FFA) levels were measured before ingestion and 60 and 180 minutes after ingestion. In addition, blood high-sensitivity CRP (h-CRP) and urinary 8-hydroxydeoxyguanosine (8-OHdG) levels were measured. Urinary 8-OHdG was corrected with urinary creatinine. Plasma triglyceride and FFA levels were measured using enzymatic methods (BML, Tokyo, Japan). The measurements of h-CRP and urinary 8-OHdG were performed with enzyme-linked immunosorbent assay methods (SRL, Tokyo, Japan). The incremental area under the curve (IAUC) of blood glucose concentration was calculated by the trapezoidal method [11] from the blood glucose concentration up to 180 minutes, with the value at fasting state as baseline.

Assessment by CGM

Two types of diets were prepared. In both types, side dishes were identical, and the staple food was WR or BR. These diets were served 3 times a day for 2 consecutive days. The daily calorie intake was adjusted to 1,800 kcal for males and 1,600 kcal for females with identical content and number of side dishes. In the case of 1,600 kcal diet a day, WR diet contained 1,677 kcal and 64.5 g protein, 47.1 g lipid, and 241 g carbohydrate (glucose 232.5 g and dietary fiber 7.2 g), while that of the BR diet was 1,602 kcal, 65.1 g protein, 47.7 g lipid, and 226 g carbohydrate (glucose 209 g and dietary fiber 16.9 g). In the case of 1,800 kcal diet a day, the amount of protein and lipid were identical to 1,600 kcal diet, but the amount of carbohydrate and dietary fiber were different. In WR diet the amount of carbohydrate was 291g (glucose 280g, dietary fiber 8.6g), while that of BR diet was 276g (glucose 250g and dietary fiber 20.3g). This study was conducted by a cross-over design. The subjects were divided into 2 groups and each group took the WR diet or BR diet in turn on the first day.

Medtronic iPro®2 (Medtronic, Dublin, Republic of Ireland) was used for CGM, which was attached to the subjects before lunch on the day before the test. Daily mean blood glucose (MBG) levels, 24-hour standard deviation of blood glucose (24-hour SDBG) and mean amplitude of glucose excursion (MAGE) [21], an index of glycemic variability calculated from the value larger than 1 standard deviation (SD) from the mean glycemic values ± SD, were analyzed.

Statistical analysis

The results were expressed as mean ± SD. Temporal changes in blood glucose, triglyceride, FFA, h-CRP, and urinary 8-OHdG were analyzed by repeated measures analysis of variance.

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Statistical significance was determined by comparing the WR diet with the BR diet before and after ingestion by paired t-test. In this study, the difference was regarded as significant if $p < 0.05$ in a 2-sided test. Statistical software SAS JMP version 11 (SAS Institute, Cary, NC, USA) was used for statistical analysis.

RESULTS

Meal tolerance test

Blood glucose increased, reached its peak value 30 minutes after ingestion of the WR diet, and returned to baseline 180 minutes after ingestion. After ingestion of the BR diet, blood glucose similarly increased and reached its peak value 30 minutes after ingestion, but the peak value was significantly lower than that of the WR diet ($p < 0.01$) (**Table 1**). The IAUC over 180 minutes after ingestion of the WR diet was 3,209.0 ± 1,951.4 mg·min/dL, whereas it was 2,352.0 ± 1,186.1 mg·min/dL for the BR diet, which was a significantly lower value ($p < 0.05$) (**Figure 1**).

Blood triglyceride levels increased significantly ($p < 0.001$) and reached a peak 180 minutes after ingestion of the WR and the BR diets. However, there was no significant difference between the WR and the BR diet. The FFA value 180 minutes after ingestion significantly decreased compared with the value before ingestion ($p < 0.001$). The value of the BR diet was significantly higher compared with that of the WR diet ($p < 0.05$) (**Table 2**). Urinary 8-OHdG significantly increased 180 minutes after ingestion of the WR diet (1.82 ± 1.11 ng/mL/Cr) compared to the value before ingestion (1.42 ± 0.65 ng/mL/Cr) ($p < 0.05$); however, no significant elevation was observed after ingestion of the BR diet (**Figure 2**). No significant changes were seen in h-CRP after ingestion of the WR diet or BR diet.

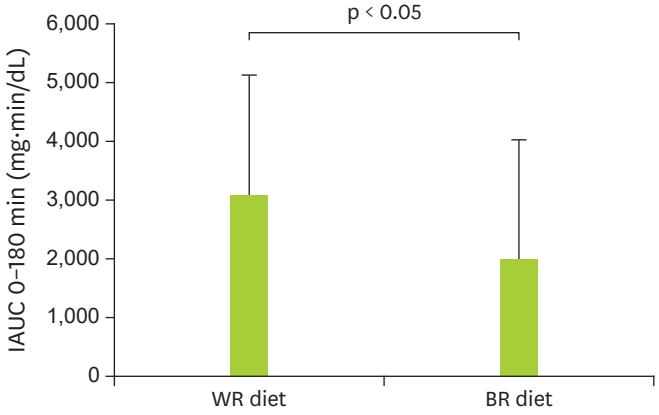

Figure 1. The IAUC of blood glucose over 180 minutes after WR diet or BR diet.
IAUC, incremental area under the curve; WR diet, only white rice as staple food; BR diet, white rice mixed with 50% β-glucan rich barley as staple food.

Table 1. Changes in plasma glucose levels after the consumption of WR diet or BR diet

Time	0 min	30 min	60 min	120 min	180 min
WR diet plasma glucose, mg/dL	90.3 ± 8.1	121.1 ± 19.4*,†	115.3 ± 22.0†	105.8 ± 12.2†	93.1 ± 13.9†
BR diet plasma glucose, mg/dL	90.1 ± 9.1	108.5 ± 12.1*,†	107.5 ± 16.2†	99.6 ± 13.0†	93.1 ± 11.4†

Data are mean ± standard deviation.
WR diet, only white rice as staple food; BR diet, white rice mixed with 50% β-glucan rich barley as staple food.
*The $p < 0.01$, WR diet vs. BR diet; †$p < 0.001$, before vs. after meal.

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Table 2. Changes in plasma lipid levels after WR diet or BR diet

Variables	Meal tolerance test	0 min	60 min	180 min
Triglyceride, mg/dL	WR diet	75.3 ± 29.9	78.5 ± 31.4	98.2 ± 51.7*
	BR diet	83.1 ± 30.7	84.1 ± 31.3	113.7 ± 47.6*,†
FFA, mEq/L	WR diet	0.52 ± 0.23	0.21 ± 0.07*,†	0.18 ± 0.09*,†
	BR diet	0.61 ± 0.23	0.23 ± 0.08*,†	0.26 ± 0.12*,†

Data are mean ± standard deviation.
WR diet, only white rice as staple food; BR diet, white rice mixed with 50% β-glucan rich barley as staple food; FFA, free fatty acid.
*The $p < 0.01$; †$p < 0.001$, before vs. after meal.

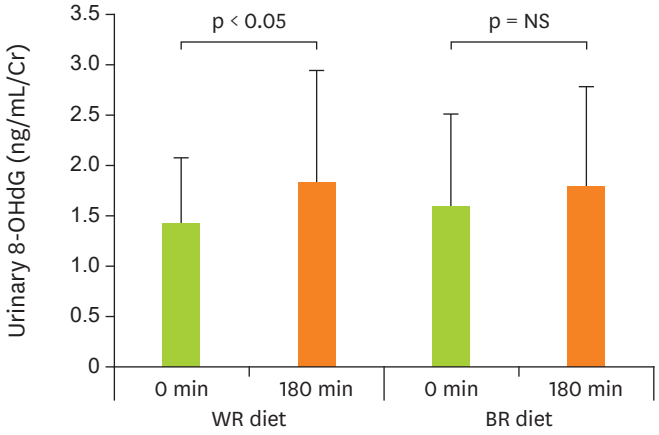

Figure 2. Changes in urinary 8-OHdG levels after test meals with WR diet or BR diet.
8-OHdG, 8-hydroxydeoxyguanosine; WR diet, only white rice as staple food; BR diet, white rice mixed with 50% β-glucan rich barley as staple food.

Assessment by CGM

MBG significantly decreased from 94.7 ± 7.8 mg/dL for the WR diet to 91.3 ± 7.8 mg/dL for the BR diet ($p < 0.01$). The 24-hour SDBG also significantly decreased from 11.3 ± 4.2 mg/dL to 8.4 ± 4.0 mg/dL ($p < 0.01$), but there was no significant difference in MAGE (**Table 3**).

DISCUSSION

Dietary fiber is divided into water-soluble and insoluble dietary fiber. Insoluble dietary fiber improves bowel movement by increasing stool volume [22], and water-soluble dietary fiber which mixes with food inside the intestine, suppresses acute glucose elevation as well as serum cholesterol elevation due to slow movement of water-soluble dietary fiber within the intestine [23,24]. It is known that water-soluble dietary fibers, especially β-glucan, strongly delay the digestion and absorption of nutrients due to its high viscosity [25]. The β-glucan accounts for a large part of the water-soluble dietary fiber of barley, and even pearled and

Table 3. The daily variation of blood glucose in CGM after consumption of WR diet or BR diet

Variables	WR diet	BR diet
24-hour MBG, mg/dL	94.7 ± 7.8	91.3 ± 7.7*
24-hour SDBG, mg/dL	11.3 ± 4.2	8.4 ± 4.0*

Data are mean ± standard deviation.
CGM, continuous glucose monitoring; WR diet, only white rice as staple food, BR diet, white rice mixed with 50% β-glucan rich barley as staple food; MBG, mean blood glucose; SDBG, standard deviation of blood glucose.
*The $p < 0.01$. WR diet vs. BR diet.

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rolled barley contains more than 19 times more dietary fiber than polished rice, which may indicate that the content of β-glucan in barley is higher than that of other grains [25,26]. This is because β-glucan is distributed in the cell wall of the barley's endosperm and high amounts of dietary fiber remain in the edible part after pearling [20]. Conventionally, β-glucan contained in barley is reported to be 4.7 g per 100 g, but the content of β-glucan in the Kirarimochi barley used in this study was as high as 7.2 g per 100 g [20].

The area under the blood glucose curve over 180 minutes in the meal tolerance test was significantly suppressed, even in the subjects with normal glucose tolerance who ingested the BR diet. The effects of the barley β-glucan on delayed digestion and absorption as well as delayed gastric emptying may contribute to the suppression of acute glucose elevation after ingestion [23,24]. The daily variation of blood glucose in CGM demonstrated that the MBG levels and 24-hour SDBG, which is an indicator of daily blood glucose fluctuation, were significantly suppressed by the BR diet. This finding seems to suggest that the barley's β-glucan suppressed the elevation of postprandial blood glucose levels. It is possible that addition of barley or similar cereals to rice, a high GI food, may lower the GI and treat postprandial hyperglycemia. The finding that mixing barley with WR improves postprandial blood glucose elevation may lead to prevention of diabetes and metabolic syndrome [27]. It has recently been shown that fermentable fiber protects against metabolic syndrome by nourishing microbiota [28]. It is also reported that meals including vegetables and dietary fiber increase glucagon-like peptide-1 as compared with WR alone and suppress hyperglycemia and excess secretion of endogenous insulin after meals [29].

It is reported that water-soluble dietary fiber has a serum cholesterol-lowering effect, a triglyceride-lowering effect as well as an improvement on intrahepatic lipid accumulation [30]. It is said that the barely-mediated increase in fecal bile acid excretion enhances the metabolism of cholesterol to bile acid in the liver and decreases blood cholesterol as a result of the decrease in liver cholesterol [26,30]. In this study, serum triglyceride levels 180 minutes after ingestion of the BR diet were even higher than those of the WR diet. In addition, there were no significant differences in the postprandial decrease in blood FFA between the WR diet and BR diet and no short-term effects on lipid concentration were observed. However, it is reported that ingestion of β-glucan-containing barley improves not only blood glucose and lipid levels but also oxidative stress [31]. In the present study, urinary 8-OHdG, which is the biomarker of oxidative stress, increased after ingestion of the WR diet, however, no significant elevation was observed after ingestion of the BR diet. These results revealed that β-glucan-containing barley improved oxidative stress via suppression of postprandial hyperglycemia. No significant changes were observed in h-CRP. Long-term utilization of barley in the diet may prevent macrovascular complications, but there is no data on the long-term effects of barley to prevent arteriosclerosis or blood glucose levels, and thus requires further investigation.

According to a report on the effective amount of barley β-glucan per serving [25,26], ingesting 4 g of β-glucan relative to 30–80 g of glucose suppresses postprandial hyperglycemia. In the BR diet in the present study, 75 g of steamed WR and steamed 75 g of Kirarimochi were contained in 150 g of the staple food, which is equivalent to 5.4 g of β-glucan per approximately 30 g of glucose in the staple food per 1 serving. This seems to be consistent with the report by Tosh [25], who recommend at least 3 g of β-glucan per serving to suppress postprandial blood glucose [25].

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CONCLUSION

In the meal tolerance test, the peak plasma glucose levels and IAUC for glucose over 180 minutes were significantly decreased by the consumption of WR mixed with 50% high β-glucan-containing barley in subjects with normal glucose tolerance. In CGM, 24-hour MBG and 24-hour SDBG were also significantly decreased after ingestion of the BR diet. Postprandial glucose elevation was suppressed by mixing high-β-glucan barley to WR in subjects with normal glucose tolerance. From this, we have concluded that lowering GI of WR, suppresses blood glucose fluctuation in individuals with normal glucose tolerance and can eventually reduce obesity and suppress the onset of diabetes for Asians who consume WR as a staple food. However, further research is needed to clarify whether high-β-glucan barley improves postprandial blood glucose in the long term or not.

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