Long-Term Effects of High Dietary Fiber Intake on Glucose Tolerance and Lipid Metabolism in GK Rats: Comparison Among Barley, Rice, and Cornstarch

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Whether the intake of high dietary fiber may improve glycemic control in individuals with type 2 diabetes has been controversial. This study was conducted to observe the long-term effects of dietary fiber intake on glucose tolerance and lipid metabolism in rats. Thirty male type 2 diabetic model GK rats were divided randomly into 3 groups. Each group was fed either a barley (high-dietary fiber) diet, rice (low-dietary fiber) diet, or cornstarch (very–low-dietary fiber) diet. The rats were pair-fed for 9 months. The intake of the barley diet significantly improved the area under the plasma glucose concentration time curves, lowered the fasting plasma glucose and glycosylated hemoglobin levels, and decreased plasma total cholesterol (T Chol), triglycerides (TG), and free fatty acid (FFA) levels. This study demonstrated that long-term intake of barley has beneficial effects on glucose tolerance and lipid metabolism and suggests the intake of unrefined cereal foods should increase as a diet therapy for type 2 diabetes.

IN THE PAST several decades, the prevalence of type 2 diabetes mellitus has been increasing in western countries[1] and Japan.[2] Westernization of dietary habits was suggested to be one of the important factors contributing to the increasing incidence of diabetes mellitus.[3] Several large-scale prospective studies showed that diets with high dietary fiber and low glycemic load were inversely related to the prevalence of type 2 diabetes in humans.[4-6] However, daily intake of dietary fiber in Japan decreased from 23 g in 1955 to 16 g in 1995,[7] which corresponds to the value in the US, 17 g in 1994.[8] Although patients with diabetes are advised to increase their intake of dietary fiber, their average daily intake was found to be only 16 g.[8]

The results of previous studies that evaluated the role of dietary fiber on blood glucose control in patients with type 2 diabetes were inconsistent.[9,10] In several studies, an improvement in blood glucose control was reported to be associated with an increase in the fiber content of the diet.[11-16] In some of these studies, the high-fiber diet had a lower fat and higher carbohydrate content than the low-fiber diet.[13,14] In other studies, there was body weight loss during the high-fiber diet in some results.[12,16] Thus, it is difficult to interpret the results described above.

In a recent cross-over study, Chandalia et al[17] treated a group of 13 obese type 2 diabetic patients with a standard American Diabetes Association (ADA)-recommended diet containing about 24 g fiber/d, in which 8 g was soluble fiber,[18] and a diet containing about twice as much total fiber, and 3 times the soluble fiber. Each diet was given for 6 weeks. The results showed the high-fiber diet improved glycemic control, as evident by decreases in the mean daily preprandial and 24-hour plasma glucose concentrations. In addition, the diet lowered 24-hour plasma insulin concentrations and also lowered glycosylated hemoglobin values slightly. There was no body weight loss during the high-fiber diet consumption.[17]

On the other hand, several studies were conducted in which an increased fiber content showed no effect.[19-21] Therefore, whether ingestion of large amounts of fibers leads to a salutary effect on blood glucose control in individuals with diabetes remains doubtful.

We confirmed that the high carbohydrate intake improved glucose tolerance compared with low carbohydrate intake.[22] To our knowledge, barley contains large quantities of dietary fiber (soluble fiber and insoluble fiber), β-glucan and is rich in carbohydrates.[10] It becomes an ideal food as a dietary fiber supplement and can be expected to be useful for blood glucose control in individuals with diabetes. In this study, we used barley, rice, and cornstarch diets, which contained similar amounts of carbohydrate, fat, and protein, but different amounts of fiber, to observe the long-term effects of dietary fiber on the glucose tolerance and lipids metabolism in GK rats.

MATERIALS AND METHODS

Animals and Diet

Thirty 7-week-old male GK rats (type 2 diabetic model rat; Nippon Clea, Tokyo, Japan) were used in the experiments. They were individually housed in stainless steel wire-bottomed cages in an air-conditioned room (22°C ± 2°C, 55% ± 10% relative humidity) with artificial lighting from 6 AM to 6 PM. For acclimation, the rats were maintained on commercial powder food (CE-2, Nippon Clea) and water ad libitum for 2 week. At 9 weeks of age, the rats were switched randomly to 3 kinds of diet: barley diet (Hakubaku, Yamanashi, Japan), rice diet (Gunma Seihun, Gunma, Japan), and cornstarch diet (Honen, Tokyo, Japan). The 3 kinds of diets were prepared as a powder. The compositions are shown in Table 1. The 3 kinds of diets were adjusted to contain the same amounts of fat, carbohydrate, protein, minerals, and vitamins. The amounts of fiber were different among the 3 diets. Each group of rats was pair-fed on the 3 kinds of diet for 9 months. The average energy intake was 80 kcal/rat/d. The food was replenished daily at 6 PM. Animals consumed their daily ration until 10 AM the next day. The consumption of food was measured once a week, and the status of the excrements was observed each day. The body weight of rats was measured once per week at a specific time in the afternoon.

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Submitted December 28, 2002; accepted March 14, 2003.

Supported by Haku-Baku Co Ltd, Yamanashi, Japan.

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0026-0495/03/5209-0047$30.00/0

doi:10.1016/S0026-0495(03)00159-8

Table 1. Composition of the Test Diets

Constituent	Barley	Rice	Cornstarch
Carbohydrate (% of total energy)	70	70	70
Protein (% of total energy)	20	20	20
Fat (% of total energy)	10	10	10
Saturated	1.4	1.4	1.4
Monounsaturated	5.2	5.2	5.2
Polyunsaturated	3.4	3.4	3.4
Fiber (g/d/rat)			
Total	1.79	0.46	0.24
Insoluble*	0.68	0.001	0
Soluble*	1.11	0.459	0.24
β-glucan†	0.7	0	0

*Insoluble and soluble dietary fiber analyzed according to a gravimetric method.

†β-glucan analyzed according to an enzymatic method.

The experiments were performed in accordance with the Guidelines for Animal Experiments of the Yamanashi Medical University, which concur with the US National Institutes of Health Guidelines.

Oral Glucose Tolerance Test

An oral glucose tolerance test (OGTT) was performed every month. All rats fasted for 6 hours before OGTT. Glucose (2 g/kg body weight) was administered orally, and blood was taken from the tail vein at 0, 30, 60, and 120 minutes for the measurement of plasma glucose and insulin concentrations. Plasma glucose was determined with a commercial CII-test kit (Wako Pure Chemical, Osaka, Japan), and plasma insulin levels were determined with enzyme-linked immunosorbent assay (ELISA) using a commercial Glazyme insulin enzyme immunoassay (EIA) test kit (Morinaga, Yokohama, Japan). The increment in plasma glucose after the glucose load was expressed in terms of the area under the plasma glucose concentration time curve (AUC) from the time when the fasting blood was drawn until the 120-minute postload blood sampling,using the trapezoidal rule.

Insulinogenic Index

An insulinogenic index (II) defined as the ratio of the change in circulating insulin to the change in the corresponding glycemic stimulus[23] was calculated using the equation: (30-min plasma insulin–fasting plasma insulin)/(30-min plasma glucose–fasting plasma glucose).

Biochemical Examination

The biochemical examination was performed every month after a 6-hour fast at specified intervals. Fasting blood was collected in hematocrit tubes from an incision on the tail vein of the rats, and the plasma was collected. Plasma total cholesterol (T-Chol), triglycerides (TG), free fatty acid (FFA) concentrations, and blood glycosylated hemoglobin levels (HbA_{1c}) were determined with commercial test kits (Wako Pure Chemical).

Statistical Analyses

Results are expressed as the means ± SD. The data were analyzed using 2-way analysis of variance (ANOVA) using the software program StatView 5.0 (Abacus Concepts, Berkeley, CA). Fisher's protected least significant difference test was used when there was a significant difference among groups. The .05 level of probability was used as the criterion of significance.

RESULTS

General Observations

Slight diarrhea was observed in some GK rats kept on the barley diet in the first 2 weeks. However, this phenomenon was diminished after acclimation. No side effects were seen in the rats fed the rice and the cornstarch diets. There were no significant differences in body weights among the 3 groups (Fig 1).

Effect of Diet on OGTT

The results of OGTT are shown in Fig 2. There was no significant difference in the first month among the 3 groups. From month 2 to month 9, the plasma glucose of rats kept on the barley diet significantly decreased at 30 and 60 minutes compared with the rats fed the rice and cornstarch diets. The AUC in the rats on the barley diet was also significantly lower than that of the rats on the rice and the cornstarch diet from month 2 to month 9 (Table 2).

Effects of Diet on Fasting Plasma Glucose, II, and HbA_{1c}

In the first month, fasting plasma glucose (FPG) showed no significant difference among the rats on the 3 diet regimens. However, FPG in the barley group was lower compared with that of the cornstarch diet group at the second month and was lower than that of both the rice and the cornstarch diet groups at the third month (Fig 1 and Table 2).

There were no significant differences in the II values among the 3 groups (Table 2).

The HbA_{1c} value was significantly lower in the rats on the barley diet than that in rats on the rice and cornstarch diets from month 3 to month 9 (Table 2).

Effect of Diet on T-Chol, TG, and FFA

The plasma T-Chol of the barley diet group at the first month was significantly lower than that of the cornstarch diet group. From the second to ninth month, the T-Chol in the barley diet group significantly decreased compared with that in the rice

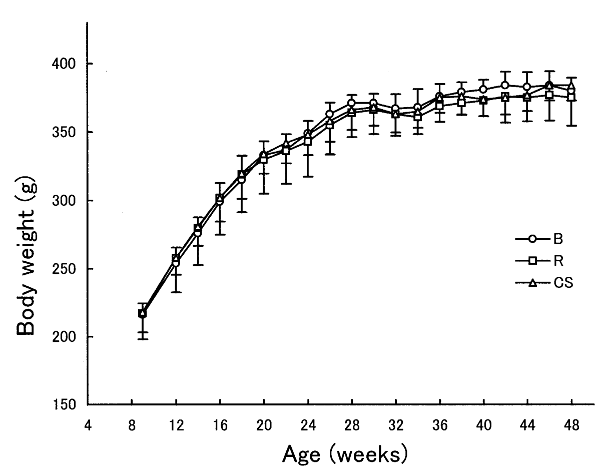

Fig 1. Body weight changes after barley (B), rice (R), and cornstarch (CS) diet feeding for 9 months in GK rats. Values are means ± SD (n = 10).

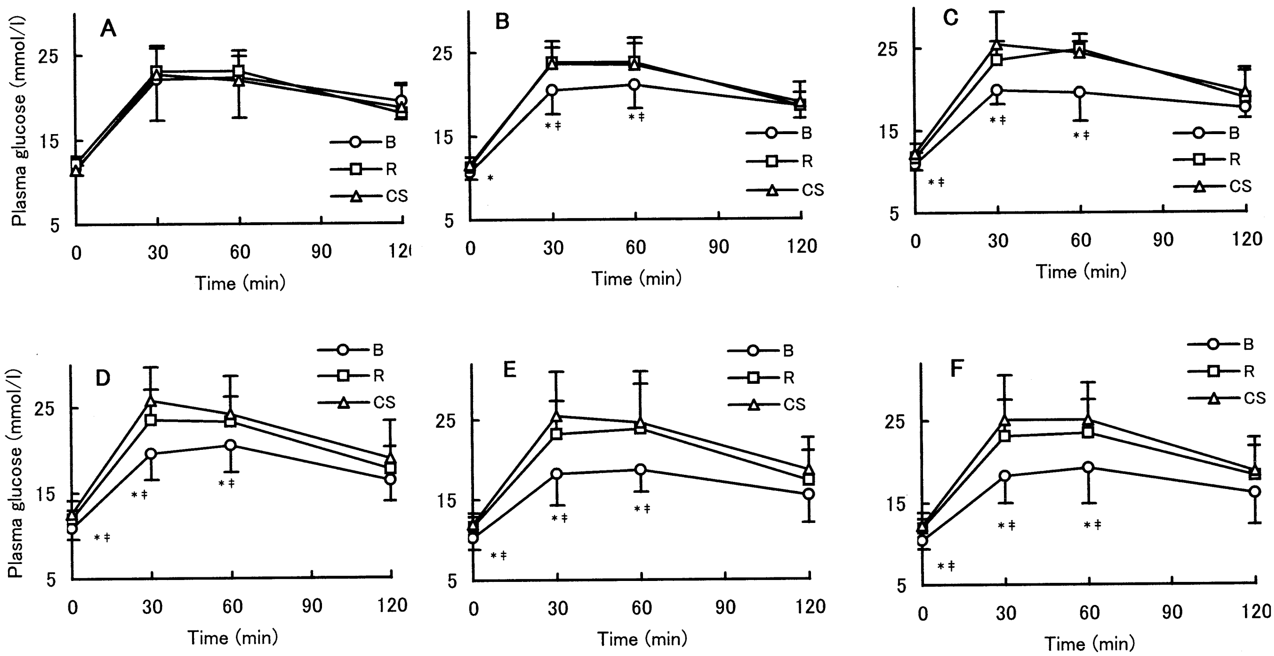

Fig 2. Plasma glucose responses to oral glucose load in GK rats fed B, R, and CS for 9 months. (A) Month 1; (B) month 2; (C) month 3; (D) month 5; (E) month 7; and (F) month 9. Values are means ± SD (n = 10). *Significantly different from R; ‡significantly different from CS.

and cornstarch diet groups. From the third to ninth month, the T-Chol in the rice diet group was lower than that in the cornstarch diet group (Table 3).

The TG in rats on the barley diet significant decreased from the first month to month 9 compared with that in rats on the rice and cornstarch diets. Moreover, the TG in the rice diet group was lower than that in the cornstarch diet group at month 7 (Table 3).

The FFA in rats on the barley diet was lower than in rats on the cornstarch diet at the second month and was lower than the rats on both the rice and cornstarch diets from the fifth to ninth month (Table 3).

DISCUSSION

Despite the controversial results of previous studies whether or not high dietary fiber is beneficial to glycemic control, the

Table 2. Effects of B, R, and CS Diet Feeding on FPG, AUC, II, and Blood HbA_{1c} Values in GK Rats

	Before	Month 1	Month 2	Month 3	Month 5	Month 7	Month 9
FPG (mmol/L)							
CS	11.9 ± 1.3	11.5 ± 0.6	11.6 ± 0.9	12.3 ± 1.2	12.6 ± 1.5	12.0 ± 1.4	12.2 ± 1.6
R	11.3 ± 1.7	12.2 ± 0.9	11.3 ± 0.6	11.7 ± 0.7	12.0 ± 1.0	11.7 ± 1.2	11.9 ± 1.2
B	11.1 ± 1.0	11.6 ± 0.7	10.7 ± 0.8*	11.0 ± 0.7*†	10.9 ± 1.3*†	10.3 ± 1.5*†	10.4 ± 1.1*†
AUC (mmol/L × h)							
CS	41.3 ± 6.7	40.1 ± 5.2	41.8 ± 2.8	44.0 ± 4.7	43.7 ± 7.0	43.5 ± 9.4	43.8 ± 8.1
R	41.9 ± 2.8	41.0 ± 4.4	41.9 ± 4.2	42.8 ± 2.6	41.0 ± 4.5	41.1 ± 7.7	41.3 ± 4.7
B	39.9 ± 3.6	40.4 ± 4.1	37.9 ± 4.0*†	36.3 ± 3.9*†	36.1 ± 5.0*†	33.5 ± 5.5*†	34.1 ± 6.5*†
II (U/mg)							
CS	4.47 ± 2.1	4.90 ± 1.9	4.21 ± 1.4	4.41 ± 1.5	4.54 ± 1.2	4.66 ± 1.4	4.95 ± 2.3
R	4.61 ± 1.8	4.87 ± 1.5	5.09 ± 2.2	5.12 ± 0.9	5.18 ± 1.2	5.23 ± 1.7	5.31 ± 2.2
B	4.52 ± 2.0	4.78 ± 1.9	5.10 ± 1.5	6.31 ± 2.7	6.34 ± 2.8	6.32 ± 3.0	6.37 ± 2.1
HbA_{1c} (%)							
CS	6.27 ± 1.7	7.45 ± 0.6	7.78 ± 1.5	9.03 ± 2.0	9.16 ± 2.8	8.80 ± 1.6	8.53 ± 1.3
R	6.62 ± 0.9	7.32 ± 0.5	7.25 ± 1.4	8.42 ± 1.1	8.78 ± 2.3	9.55 ± 2.9	9.10 ± 2.5
B	6.44 ± 1.0	6.92 ± 1.2	6.81 ± 1.0	7.41 ± 0.6*†	7.02 ± 1.2*†	7.36 ± 1.3*†	7.23 ± 1.2*†

NOTE. Values represent means ± SD for 10 rats.

Abbreviations: B, barley; R, rice; CS, cornstarch; FPG, fasting plasma glucose; AUC, area under the plasma glucose concentration time curves; II, insulinogenic index; HbA_{1c}, glycosylated hemoglobin.

*$P < .05$ B *v* S.

†$P < .05$ B *v* R.

Table 3. Effects of B, R, and CS Diet Feeding on Plasma T-Chol, TG, and FFA Values in GK Rats

	Before	Month 1	Month 2	Month 3	Month 5	Month 7	Month 9
T-Chol (mmol/L)							
CS	2.91 ± 0.8	3.35 ± 0.4	3.88 ± 0.4	4.34 ± 0.5	4.61 ± 0.6	4.53 ± 0.7	4.62 ± 0.5
R	2.86 ± 0.6	2.99 ± 0.7	3.56 ± 0.3	3.75 ± 0.5‡	3.86 ± 0.5‡	3.92 ± 0.7	3.98 ± 0.5‡
B	2.87 ± 0.5	2.96 ± 0.4*	3.23 ± 0.4*†	3.31 ± 0.4*†	3.24 ± 0.3*†	3.13 ± 0.4*†	3.32 ± 0.5*†
TG (mmol/L)							
CS	0.93 ± 0.3	1.07 ± 0.2	1.10 ± 0.2	1.14 ± 0.2	1.23 ± 0.2	1.28 ± 0.2	1.13 ± 0.2
R	0.90 ± 0.2	1.07 ± 0.2	1.12 ± 0.3	1.16 ± 0.3	1.11 ± 0.2	1.18 ± 0.3‡	1.04 ± 0.2
B	0.91 ± 0.3	0.83 ± 0.1*†	0.88 ± 0.2*†	0.92 ± 0.2*†	0.90 ± 0.2*†	0.84 ± 0.2*†	0.86 ± 0.1*†
FFA (Eq/L)							
CS	625 ± 101	658 ± 99	738 ± 117	745 ± 135	729 ± 101	768 ± 117	844 ± 147
R	613 ± 95	646 ± 57	718 ± 164	736 ± 154	739 ± 138	742 ± 106	775 ± 104
B	620 ± 83	611 ± 79	634 ± 88*	652 ± 108	614 ± 93*†	631 ± 125*†	699 ± 68*†

NOTE. Values represent means ± SD for 10 rats.

Abbreviations: T-Chol, total cholesterol; TG, triglyceride; FFA, free fatty acid.

*$P < .05$ B *v* S.

†$P < .05$ B *v* R.

‡$P < .05$ S *v* R.

present study found that the intake of barley (high dietary fiber) significantly improved glucose tolerance (Fig 2) and lowered FPG and HbA_{1c} levels (Table 1) in the high carbohydrate diet condition in GK rats. This finding is consistent with those of several studies that reported an increase in the intake of total dietary fiber (predominantly soluble fiber) significantly improved glycemic control and decreased the degree of hyperinsulinemia in patients with type 2 diabetes.[16,17,24]

The relationships between improved glycemic control and high fiber intake remain undefined. Barley is known to contain an abundance of soluble and insoluble fiber. The endosperm cell walls of barley rich in β-glucan, a polysaccharide formed by linear chains with β-1,3 and β-1,4 linkages. The β-glucan is partially soluble and highly viscous in the soluble condition.[10,25] Probably, the β-glucan reduces glucose and insulin levels by increasing the viscosity of the contents of the stomach and small intestine, which decreases the absorption of digested nutrients from the small intestine.[26] Glucose transport in the intestinal wall is inhibited partly by an increased resistance of the mucosal diffusion barrier brought about by the greater viscosity of the intestinal bolus.[10] Thus, the lengthening of carbohydrate digestion and absorption appears to be the major factor responsible for the lower plasma glucose response.[27] In patients with type 2 diabetes, early-phase insulin release is deficient.[28] Carbohydrates with high fiber content may delay the absorption of glucose, thereby permitting a better match between the timing of insulin release and peak blood glucose concentrations.[29] It can be thought that β-glucan shows a similar effect with treatment of other agents, such as α-glycoside inhibitors. Another possibility is soluble fiber may be fermented by intestinal bacteria to short-chain fatty acids, such as acetate, propionate, and butyrate, which reduce plasma glucose.[30]

On the other hand, dietary fiber can significantly alter proglucagon gene expression and modulate glucagon-like peptide-1 (GLP-1) and insulin secretion.[31] GLP-1 has a significant role in the disposition of glucose absorbed from the gut. Circulating GLP-1 has a regulatory effect on basal islet output of glucagon and consequently fasting glycemia.[32] In addition, enhanced consumption of soluble fiber improves blood glucose disposal by increasing skeletal muscle plasma membrane GLUT-4 content.[33] Therefore, these possible mechanisms may explain that high dietary fiber not only improved postprandial glucose, but also lowered FPG levels and improved the glucose tolerance.

In the present experiment, the barley diet (high dietary fiber) improved the lipid metabolism, as evident by the lower T-Chol, TG, and FFA levels compared with that of the rice (low-dietary fiber) and cornstarch (very–low-dietary fiber) diets (Table 3). Several studies showed that the lowering of cholesterol can be attributed to the intake of high soluble fiber,[17,34,35] increased excretion of bile acids or neutral sterols,[36] increased catabolism of low-density lipoprotein cholesterol,[37] and reduced fat absorption.[38] Soluble fibers have been shown to be fermented in the colon giving rise to short-chain fatty acids, which can be absorbed and may inhibit hepatic cholesterol synthesis.[34] It was also reported that the amount of dietary fiber showed no effects on plasma TG in some studies with normal and hypercholesterolemic subjects.[34,39] However, the plasma TG concentration decreased in the high-dietary fiber diet in the present study. In addition, the FFAs were lower in rats kept on the diet with high dietary fiber. Fatty acids may induce insulin resistance. Thus, the lower insulin resistance will benefit blood glucose control.[29]

In the present experiment, there was no significant difference in FGP and glucose tolerance during the first month among the 3 diet groups (Fig 2 and Table 1) . These results suggested that dietary fiber intake over a short term do not influence FGP and glucose tolerance. It is possible that the mechanism of improvement in FGP and glucose tolerance is not the same as that of postprandial glucose.

The amount of dietary fiber in the barley diet was 1.79 g/d/rat. This amount is very high when converted to humans (45 to 72 g/d). However, this dose intake is approximately consistent with the dose intake recommended by Chandalia et al[17] and benefits blood glucose control.

In this experiment, we also used a control group. The amount of dietary fiber in the control group diet was 0.9 g/d/rat. Consequently, it was better than the rice and cornstarch diets, which was worse than the barley diet. However, the control group diet used a commercial powder food (CE-2, Nippon Clea). Because some food components (ratio of soluble and insoluble fiber and quantity of β-glucan) are not exhibited by the company, it is difficult to compare directly.

In conclusion, the results of the present study demonstrated that long-term intake of high dietary fiber has beneficial effects for blood glucose control, glucose tolerance, and lipid metabolism in GK rats. Therefore, these results suggest that diet therapy for patients with type 2 diabetes mellitus should increase intake of dietary fiber, particularly the consumption of unrefined cereal foods.

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