Eur J Nutr (2009) 48:170–175
DOI 10.1007/s00394-009-0778-3

ORIGINAL CONTRIBUTION

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Glucose and insulin responses to whole grain breakfasts varying in soluble fiber, β-glucan

A dose response study in obese women with increased risk for insulin resistance

Received: 8 October 2008
Accepted: 15 January 2009
Published online: 5 February 2009

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Abstract *Background* A high intake of whole grains containing soluble fiber has been shown to lower glucose and insulin responses in overweight humans and humans with type 2 diabetes. *Aim of the study* We investigated the linearity of this response after consumption of 5 breakfast cereal test meals containing wheat and/or barley to provide varying amounts of soluble fiber, β-glucan (0, 2.5, 5, 7.5 and 10 g). *Methods* Seventeen normoglycemic, obese women at increased risk for insulin resistance consumed 5 test meals within a randomized crossover design after consuming controlled diets for 2 days. Blood samples for glucose and insulin response were obtained prior to and 30, 60, 120 and 180 min after consuming the test meals. *Results* Consumption of 10 g of β-glucan significantly reduced peak glucose response at 30 min and delayed the rate of glucose response. Area under the curve for 2 h-postprandial glycemic response was not affected by β-glucan content. However, peak and area under the curve of insulin responses were significantly affected by the β-glucan amount in an inverse linear relationship. *Conclusion* These data suggest that acute consumption of 10 g of β-glucan is able to induce physiologically beneficial effects on postprandial insulin responses in obese women at risk for insulin resistance.

Key words soluble fiber – obesity – β-glucan – insulin resistance – glucose

Introduction

Insulin resistance is a major risk factor for type 2 diabetes and cardiovascular disease [19]. Insulin resistance and compensatory hyperinsulinemia have been associated with hypertension, dyslipidemia, and the metabolic syndrome. Both genetic and environmental factors contribute to the development of insulin resistance. Obesity and physical inactivity are considered major risk factors for insulin resistance [19, 25, 26].

Lifestyle strategies that include dietary modification, such as increased consumption of dietary fiber found in whole grains, may improve insulin resistance [15, 20, 24]. Soluble fiber has been suggested as the component of fiber that lowers cholesterol concentrations, and regulates blood glucose and insulin

EJN 778

responses to a meal [7, 12, 22]. Studies in our laboratory have demonstrated that consumption of foods containing the soluble fiber, β-glucan from oats and barley, have beneficial effects on glucose metabolism, lipids and blood pressure in overweight and/or mildly hypercholesterolemic persons. Based on its soluble fiber content, barley may be as effective as or more effective than oats on health effects [1–5]. Increased consumption of β-glucan, found in barley, may reduce risk for insulin resistance and diabetes; however, there are few studies that have evaluated the effects of barley consumption in adults at risk for insulin resistance.

Research linking consumption of barley to risk factors for type 2 diabetes and cardiovascular disease is needed to tailor dietary recommendations. Therefore, evaluating the acute effects of consumption of barley or barley products containing β-glucan on glucose and insulin metabolism will provide data to understand the mechanism by which chronic consumption of barley/soluble fiber may contribute to the improvement of glucose and insulin responses in overweight and obese adults with insulin resistance. Recently, we conducted a pilot study that showed in overweight women, peak glucose responses and area under the curve were significantly reduced after consumption of barley cereal containing 2 g of β-glucan compared with wheat cereal (0 g of β-glucan) and/or a mixture of barley and wheat (1 g of β-glucan). In overweight men, there were no acute effects of β-glucan on glucose response [14].

This current study investigates the acute dose response effect of 5 breakfast cereal test meals, providing β-glucan from barley, at approximately 0, 2.5, 5, 7.5 and 10 g on postprandial glucose and insulin responses in obese women at increased risk for insulin resistance. The study is conducted in women because there was a demonstrated sex difference in glucose response to consumption of barley and/or wheat in our previous pilot study [15].

Materials and methods

Subjects

Women aged >25 years were recruited by advertisement from the greater Washington, DC, metropolitan area. Inclusion criteria for subjects with increased risk for insulin resistance were determined by the tree models of Stern et al. [27]; either a) body mass index (BMI) > 27.5 kg/m^2 and homeostasis model assessment of insulin resistance (HOMA-IR) = {Fasting insulin (μU/ml) × [Fasting glucose (mmol/l)/22.5]} > 3.60 [16] or b) BMI > 28.9. Subjects were excluded if they had a BMI < 27.5 kg/m^2 or reported tobacco use, recent pregnancy or lactation, history of cardiovascular disease, diabetes, kidney disease, liver disease, and certain cancers. Subjects underwent a two-phase medical screening process. First, fasting blood and urine samples were used for a general clinical screening. Second, oral glucose tolerance tests (OGTT) were performed to exclude subjects who had diabetes if plasma glucose values were greater than 11.1 mmol/l (200 mg/dl) at 1 or 2 h after consumption of 75 g of a glucose solution. Study entry was approved by a physician on the basis of the subjects' medical history, screening blood, urine and OGTT test results, and a physical examination. All subjects gave their informed consent, and the experimental protocol was approved by the MedStar Research Institute Institutional Review Board. The subjects were compensated for their participation in the study.

Design

A randomized crossover design was used to compare the dose response effect of 5 cereal breakfast test meals. Each test day was separated by a 7-days washout period. Subjects were instructed to consume at least 55% of their total energy intake as carbohydrate (≥250 g/d) for 2 days prior to the test meals. The day before the test meal, subjects were provided standardized meal and snack by the facility that contained 15% protein, 50% carbohydrate, and 35% fat. Subjects were required to consume all their food before 8 p.m. The following morning (after an 11-h fast), day 4 (test day), subjects arrived at the Beltsville Human Nutrition Research Center. Subjects provided fasting blood samples and then consumed their breakfast test meal within 10 min. Additional blood samples were collected at 30, 60, 120 and 180 min after the start of consuming the test meal for glucose and insulin analysis. Plasma glucose concentrations were measured by an automated enzymatic method (CentrifiChem System 500, Union Carbide, Trace-America, Miami, FL) using a kit (#15910, Trace-America, Allentown, PA). Plasma insulin concentrations were measured using Active®Insulin Enzyme-Linked Immunosorbent (ELISA) kit (Diagnostic Systems Laboratories, Inc. Webster, TX). Two-hour postprandial response areas under the curve (AUCs) were calculated using the trapezoid method.

Test meals

The composition of the test meals served as hot cereal is shown in Table 1. Water intake (465 g) was controlled for across all 5 breakfast cereal test meals. The

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Table 1 Content and composition of test meals

Component	Test meal				
	0 g of β-glucan	2.5 g of β-glucan	5 g of β-glucan	7.5 g of β-glucan	10 g of β-glucan
Wheat (g)	60	45	30	15	0
Barley (g)	0	16.1	32.3	48.4	64.5
Protein (g)	12.0	12.3	12.5	12.7	13.3
Carbohydrate (g)	60.8	61.5	62.2	62.9	63.6
Fat (g)	4.3	4.6	4.9	5.1	5.3
Water (g)	384.8	386.8	389.8	389.8	386.7
Weight (g)	465.3	467.8	471.7	474.2	470.3
Energy (Kcal)	335.9	340.1	344.5	348.9	353.4

calculated total dietary fiber contents for 0, 2.5, 5, 7.5 and 10 g β-glucan cereal meals were 8.8, 11.6, 14.5, 17.2 and 20.1 g, respectively. Wheat was obtained locally and barley (Sustagrain Barley™) was generously provided from ConAgra (Omaha, NE). Wheat and barley β-glucan content were determined by the mixed-linkage β-glucan streamlined method [18] using an enzymatic method (Megazyme International Ireland, Ltd., Wicklow, Ireland). An investigator monitored all test meal consumption. Subjects were required to completely consume the test meal, utilizing a spatula to empty the serving container.

Statistical analysis

Data are presented as mean ± SEM. Area under the curve was calculated using the trapezoid method for the responses to the breakfast meals for glucose and insulin. Repeated-measures analysis of variance (ANOVA) was used to determine statistically significant differences using PROC MIXED SAS®9.1.3. (SAS Institute, Cary, NC). Linear orthogonal polynormial contrasts were used to test the significance of the amount of β-glucan (0, 2.5, 5, 7.5 and 10 g) consumed. Differences between groups were determined by least significant differences using the significance of $P < 0.05$.

Results

Subject characteristics

Twenty-one women underwent the initial screening phase. Four women were excluded from the study due to abnormal glucose tolerance results obtained from the OGTT during the second phase of screening. Seventeen women completed the study and were considered to have normal glucose tolerance, however, based on Stern et al. decision tree models [27], the women in this study were classified as having a 94% probability of being insulin resistant. The mean HOMA-IR, Mffm/I and McAuley equations indicated that the subjects were insulin resistant [16, 17]. Subject characteristics are presented in Table 2.

Effects of β-glucan on glucose and insulin response

The differences in fasting plasma glucose and insulin concentrations were not significant. Consumption of 10 g of β-glucan significantly reduced peak glucose response at 30 min ($P < 0.05$) compared with 0, 2.5 and 5 g of β-glucan in obese women (Fig. 1a). However, area under the curve during a 2-h glucose re-

Table 2 Subject characteristics

Characteristic	Women (n = 17)
Age (years)	51.6 ± 2.1
Height (cm)	168.1 ± 1.2
Weight (kg)	94.3 ± 3.0
Body mass index[a]	33.2 ± 0.8
Percentage body fat (%)	45.5 ± 0.7
Waist circumference (cm)	101.4 ± 1.8
Waist-to-hip ratio	0.83 ± 0.01
Fasting plasma glucose (mmol/l)	5.7 ± 0.2
Fasting plasma insulin (μU/ml)	18.5 ± 2.3
Triglyceride (mmol/l)	2.2 ± 0.3
HDL cholesterol (mmol/dl)	1.4 ± 0.1
LDL cholesterol (mmol/dl)	3.2 ± 0.2
Systolic blood pressure (mmHg)	126.1 ± 4.2
Diastolic blood pressure (mmHg)	71.4 ± 2.8
HOMA-IR[b]	4.5 ± 0.6
Mffm/I[c]	5.3 ± 0.3
McAuley[d]	5.3 ± 0.3

All data expressed as mean ± SEM
[a]Expressed in kg/m^2
[b]Calculated by the equation {fasting insulin (uU/ml) × [fasting glucose (mmol/l)/22.5]}
[c]Calculated by the equation exp[2.63 − 0.28ln(fasting insulin) − 0.31ln(fasting triglyceride)]
[d]Calculated by equation exp[3.29 − 0.25ln(fasting insulin) − 0.22ln(BMI) − 0.28ln(fasting triglyceride)]

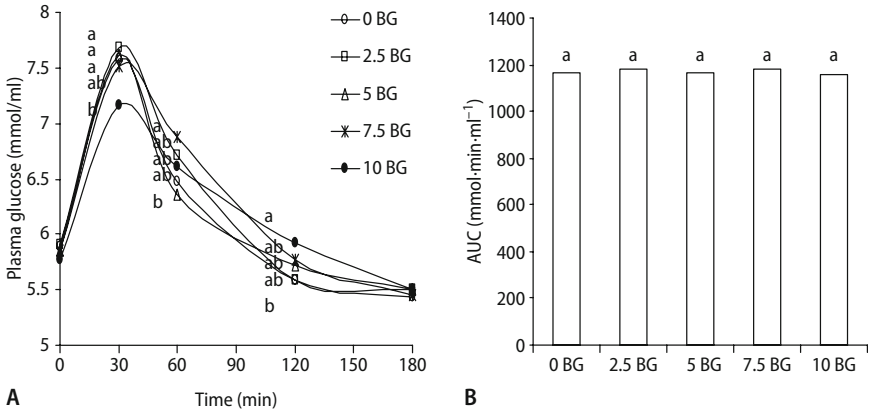

Fig. 1 Glucose response after consumption of test meals containing 0, 2.5, 5, 7.5 and 10 g of β-glucan in 17 obese women. **a** Glucose response. **b** Area under the curve (AUC) during 2-h meal tolerance test. 0 BG = 0 g of β-glucan; 2.5 BG = 2.5 g of β-glucan; 5 BG = 5 g of β-glucan; 7.5 BG = 7.5 g of β-glucan; 10 BG = 10 g of β-glucan. Data were expressed as mean. *Different letters* indicate significant difference at $P < 0.05$

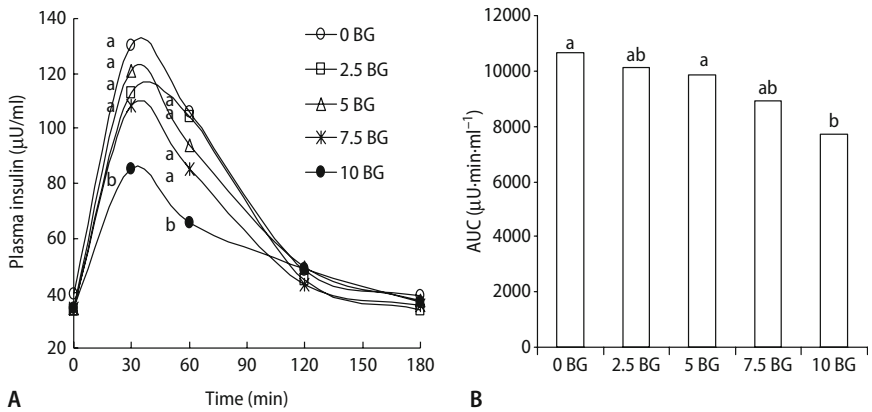

Fig. 2 Insulin response after consumption of test meals containing 0, 2.5, 5, 7.5 and 10 g of β-glucan in 17 obese women. **a** Insulin response. **b** Area under the curve (AUC) during 2-h meal tolerance test. 0 BG = 0 g of β-glucan; 2.5 BG = 2.5 g of β-glucan; 5 BG = 5 g of β-glucan; 7.5 BG = 7.5 g of β-glucan; 10 BG = 10 g of β-glucan. Data were expressed as mean. *Different letters* indicate significant difference at $P < 0.05$

sponse was not significantly different among β-glucan content (Fig. 1b).

Consumption of 10 g β-glucan resulted in a remarkable reduction of insulin response at 30 min ($P < 0.05$) and 60 min ($P < 0.05$) after consumption of test meals compared with 0, 2.5, 5 and 7.5 g β-glucan (Fig. 2a). Concomitantly, area under the curve during a 2-h insulin response ($P < 0.05$) was significantly reduced after consumption of 10 g β-glucan compared with 0 and 5 g of β-glucan (Fig. 2b). Area under the curve was decreased linearly as the amounts of β-glucan increased from 0, 2.5, 5, 7.5 and 10 g ($P < 0.03$).

Discussion

Previous studies from our laboratory and others, have demonstrated that consumption of foods naturally high in β-glucan, such as oats and barley, improved glycemic and insulin responses in overweight subjects or subjects with type 2 diabetes [1, 6, 10, 11, 13, 28, 29]. This study showed that in obese women at increased risk for insulin resistance, consumption of barley containing 10 g of β-glucan, elicited a significant reduction in insulin response during a 2-h meal tolerance test and β-glucan affected insulin response in a dose-dependent manner. However, it did not affect 2-h glucose area under the curve despite the delayed rate of plasma glucose absorption. These data suggest that consumption of 10 g of β-glucan per serving induces beneficial insulin responses in obese women with high risk for insulin resistance. Consumption of 10 g of β-glucan resulted in a significant reduction of the peak response of glucose at 30 min but less reduction between 60 and 120 min compared with 0, 2.5, 5 and 7.5 g of β-glucan, indicating a delayed rate of glucose absorption. In contrast, insulin response showed a more remarkable reduction at 30 and 60 min, resulting in a significant reduction of 2-h insulin area after consumption of 10 g of β-glucan. The subjects in the present study had normal glucose tolerance as determined by OGTT which suggests that their β-cell function to secrete insulin was not defective. Therefore, it is likely that delayed rate of glucose absorption after consumption of 10 g of β-glucan is in part associated with a reduction of insulin response (and probably with a delayed rate of gastric

emptying and the motility in the gastrointestinal tract).

A potential mechanism mediating a significant reduction in insulin response after β-glucan consumption may be related to changes of gut hormones. The effect of insulinotropic gut hormones on insulin secretion is responsible for approximately 70% of the peripheral insulin response to nutrients [21]. Plasma insulin responses were closely associated with gastric inhibitory polypeptide and glucagon-like peptide 1 responses in healthy subjects [23]. Gastric inhibitory polypeptide was reduced after consumption of diets containing guar gum and grain products [8, 9]. Additional research is required to determine whether incretin hormones such as gastric inhibitory polypeptide and glucagon-like peptide 1 are affected by consumption of β-glucan found in barley.

We conducted a previous study that showed consumption of cereal products containing 2 g of β-glucan significantly reduced postprandial glucose responses (peak glucose response and 2-h glucose area) compared with 0 g of β-glucan [14]. In contrast, the present study showed that higher amount of β-glucan consumption (10 g) induced a reduced peak and sustained net increment in the late phase (60 and 120 min) of postprandial glucose response. The possible factors for the discrepant glucose response to β-glucan may be due to either the subject population or physiological properties of β-glucan such as processing and different cooking preparation for test meals (heated and served with vs. without yogurt). The present study was designed to target obese women at risk for insulin resistance based on Stern et al. decision tree models [27]. In contrast, the previous study was conducted in insulin sensitive overweight women. Therefore, greater amounts of β-glucan per serving may be required for the management of hyperglycemia in obese women at increased risk for insulin resistance compared with insulin sensitive overweight women. A reduction of glucose concentrations at 30 min and sustained net increment at 60–120 min after consumption of 10 g β-glucan may be metabolic favorable for obese women who have high risk for development of type 2 diabetes.

Strengths and limitations of our study design warrant consideration. There were several strengths of the study. First, the choice of study design was important; this was a randomized crossover design. This is one of the most powerful designs for evaluating the efficacy of dietary treatments. Second, several measures of adherence to the treatments and the controlled diet were made. In the present study, dietary intake was controlled for 3 days prior to the dose response. All foods were provided to the subjects 24 h prior to the test days to control for other dietary confounding factors and a research dietitian monitored the subjects' treatment intake to ensure adherence to the study protocol. There were, however, several limitations to the study. The small sample size was limiting, although power calculations indicated that 14 subjects were needed to show significant changes in glucose responses. Consumption of 10 g of β-glucan in one meal is atypical and is usually consumed throughout the day at three separate eating occasions. However, the 10 g dose of β-glucan (64.5 g of Sustagrain Barley™, approximately 2.3 servings of a breakfast cereal) was well tolerated by the subjects; no adverse events were reported. Therefore, such a dose is within the possibility of consumption at one meal.

In conclusion, acute consumption of barley cereals containing the soluble fiber β-glucan reduced insulin response in a dose-dependent manner and at least 10 g of β-glucan per serving was required in obese women who have increased risk for the development of insulin resistance. High β-glucan whole grain products may prove useful in the inclusion of dietary management of hyperglycemia in obese women.

Acknowledgments We express our gratitude to the staff of the Beltsville Human Study Facility, including the research kitchen staff: Evelyn Lashley, Sue Burns, Diane Shegogue, and Mattie Long and research assistants: Willa Mae Clark, Demetria Fletcher, and Razia Hussain We acknowledge ConAgra (Omaha, NE) for generously supplying the barley. And, especially we wish to thank each volunteer for their participation and commitment to making this study possible.

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