Perturbations of blood chemistry and after the short-term feeding of a fiber supplement in noninsulin dependent diabetic and nondiabetic subjects

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Dietary fiber has important roles in lowering blood lipids and, at least for diabetic people, in controlling blood glucose. Unfortunately, mechanisms by which fiber exerts these important effects are poorly understood. The result is that one has little basis for rating the metabolic potency of fibers from their chemical or physical properties and for making specific and quantitative recommendations about fiber intakes for people. Ultimately, one needs to develop and test mechanistic models that predict how various changes in dietary fiber will affect the rate and magnitude of changes in blood lipids. The present study represents an early step toward that goal. A semi-purified fiber supplement (Fiber Excel) was added daily to the self-selected diets of a small group of noninsulin dependent diabetic and nondiabetic subjects for two weeks, and fasting bloods were taken prior to the supplement, after 1 and 2 weeks of fiber supplementation, and 1 week later. The extra fiber elicited few complaints of abdominal distress. Plasma glucose was depressed after 1 week in diabetic subjects while triglycerides were depressed after 1 and 2 weeks in nondiabetics. Total cholesterol tended to decrease ($P > 0.05$) among diabetic subjects, and the decrease was statistically significant in the high-density lipoprotein fraction in both groups. None of the parameters affected by extra fiber changed significantly within 1 week of its withdrawal. It appears that the time course of effects of adding or removing extra fiber from the diet can be observed and that these effects may persist for more than 1 week.

Keywords: fiber supplement; glycemic control; post-supplementation effect; physiological state; lipemic control; glycosylated hemoglobin

Introduction

The consumption of high fiber foods is effective in attenuating postprandial glycemic response,[1-3] lowering serum cholesterol,[4,5] and in many cases lowering serum triglyceride.[6,7] The addition of semipurified fibers has also been shown to mimic these effects.[3-7] However, the mechanism of hypolipidemic effects of fibers is not well understood. Although bile acid-binding and water-holding capacities, as well as altered micellar formation properties, have been postulated as possible mechanisms of the hypolipidemic effects of fibers, one cannot predict the hypolipemic potency of a fiber from its chemical structure or its physical properties. This makes dietary recommendations of fibers vague and non-specific.

In the present study a fiber supplement was added to the self-selected diets of diabetic and nondiabetic subjects for 2 weeks and then withdrawn. Plasma glucose and lipids were measured before and during fiber supplementation and 1 week later. The underlying

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hope was that information about the time course of the change of critical parameters when fiber intake is pertubed may provide important clues about the direct effect fiber may be responsible for in the gastrointestinal tract.

Materials and methods

Subjects

The subjects in this study had previously participated in our nutrition study entitled "Effects of dietary pattern on diseases in south west Mississippi" and had proved reliable in following directions and in keeping diet records. Eight non-insulin-dependent diabetic (NIDDM) subjects [two males and six females, mean age 50.5 yr] with a fasting blood glucose >7.8 mmol/L (140 mg/dL) and eight nondiabetic subjects (ND) (two males and six females, mean age 47) were selected for the study. The subjects were instructed not to take any medications and they were free of digestive disorders as indicated by their medical record. They maintained their usual lifestyle during the course of the study. The study protocol was approved by the Alcorn State University Committee on Protection of Human Rights.

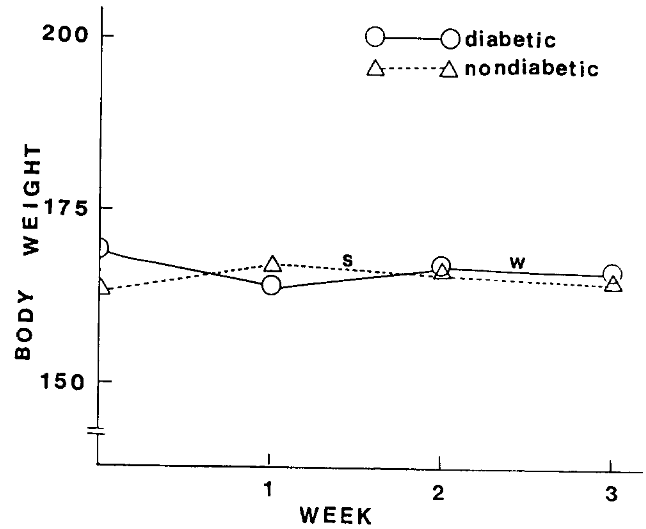

Figure 1 Body weights of diabetic and non-diabetic subjects taken on blood sampling periods. Each point represents a group mean (S = fiber supplemental period, W = fiber withdrawal period).

Protocol

The subjects were instructed by outpatient clinical personnel at The Jefferson Memorial Hospital in Natchez, MS, USA to eat their usual diets throughout the study and to consume 30 g of a fiber supplement [Fiber Excel generously supplied by Medivix Inc. (Natick, MA, USA)] daily. The supplement was taken in two portions, 15 g at breakfast and 15 g at lunch for 14 days. Bloods were taken from the antecubital vein after an overnight fast at the following four times: one week prior to the start of the study (basal sample), at the end of the first and second weeks of taking the fiber supplement (wk 1 and wk 2), and 1 week after supplementation was halted (week 3).

Detailed 3-day food intake records were kept by each subject prior to each blood sample after the study began. Nutrient intake was estimated from the diet records by the N^2 Software nutrient data base.[8] Soluble and insoluble fiber contents of the supplement were analyzed by the method of Li et al.,[9,10] *[Table 1]*.

Biochemical procedures

Fasting blood samples were obtained between 8:00 and 10:30 a.m. from the antecubital vein prior to the beginning of the study (baseline), at the end of each week of the study (wk 1 and wk 2) and 1 week after supplementation.

Glycosylated hemoglobin (HBA_{1c}) was analyzed by ion exchange chromatography followed by spectrophotometric determination,[11] plasma glucose by the *o*-toluidine procedure, total triacylglycerol (TG) by Sigma diagnostic kit (Sigma Chemical Co., St. Louis, MO, USA), total cholesterol (TC) by the cholesterol oxidase procedure. high density lipoprotein-cholesterol (HDL-C) by dextran sulfate-magnesium precipitation followed by enzymatic (cholesterol oxidase) determination, and low density lipoprotein-cholesterol (LDL-C) by difference using the following molar relationships:[12]

$$LDL\text{-}C = TC - [HDL\text{-}C + 0.46 \text{ total triglyceride } (TG)]$$

Table 1 Contents of daily intake of fiber supplement

Total weight		30 g
Total dietary fiber		12.1 g[a]
Soluble	1.7[a]	
Insoluble	10.4[a]	
Starch		5.0[b]
Protein		6.0[b]
Fat		<2.0 g[b]
Moisture		1.5 g[b]
Sodium		15 mg[b]

[a]By method of Li et al, (9, 10) with autoclaving of samples for 1 hour at 121° C to gelate starch and dissolve "soluble fiber."
[b]Values as supplied by manufacturer.

Statistical analysis

The Student *t* test was used to compare basal measurements in diabetic versus nondiabetic subjects prior to the start of the study. Data on blood components were also separately analyzed for NIDDM and nondiabetic subjects, by two-way analysis of variance with subjects and weeks as main effects. Means by weeks were compared by the Duncan Multiple Range Test.[13]

Results

Caloric and nutrient intake

During the basal week, diabetic subjects were found to have higher serum glucose and triglycerides and tended to have higher total cholesterol and LDL-C and a higher degree of glycosylation of blood hemoglobin than nondiabetic subjects *(Table 2)*. Diet records indicated that during the study diabetics consumed only about one-third the amount of sugars as nondiabetics and tended to ingest less energy. Otherwise,

Table 2 Average daily caloric and nutrient intake by week*

	Total Kcal	% Prot Cal	% Cho Cal	% Fat Cal	SFA (g)	PUFA	Cholesterol (mg)	P/S	Sugar (g)	Crude fiber (g)
					Diabetic					
Wk_1	1035 ± 255	21 ± 2.52	47 ± 7	31.8 ± 5	10.6 ± 1.0	4.6 ± 2.2	506 ± 338	0.43 ± 0.23	27.5 ± 20.6	3.6 ± 1.8
Wk_2	1161 ± 80	24.7 ± 2.3	40 ± 1.4	36 ± 7.9	15.2 ± 3.2	4.3 ± 1.9	497 ± 196	0.28 ± 0.09	22.8 ± 9.7	2.7 ± 1.0
Wk_3	1217 ± 151	24.3 ± 1.3	41 ± 1.4	34 ± 8.5	17.1 ± 4.9	3.9 ± 1.1	426 ± 46.4	0.22 ± 0.02	27.7 ± 19.9	4.2 ± 3.9
					Non-diabetic					
Wk_1	1642 ± 472	17 ± 1.5	54 ± 11.7	28 ± 7.7	14.8 ± 2.4	4.5 ± 16	238 ± 140.1	1.3 ± 1.2	74.6 ± 60.2	6.3 ± 3.2
Wk_2	1573 ± 461	19 ± 1.3	55 ± 15.4	26 ± 10.0	12.8 ± 4.8	5.3 ± 3.1	319.9 ± 233.1	0.38 ± 0.14	76.8 ± 34.5	5.5 ± 2.0
Wk_3	1414 ± 654	21 ± 10.7	53 ± 13.5	26.3 ± 7.2	11.6 ± 1.2	4.6 ± 1.2	1906.6 ± 110.0	0.44 ± 0.24	76.4 ± 95.6	6.5 ± 4.4

*Values = Mean ± SD
In general, neither diabetic or non-diabetic subjects differed significantly ($P < 0.05$) in their intake of energy or specific nutrients from week to week.

Table 3 Serum composition during basal, fiber supplemental and withdrawal periods by week*

	GLU mmol/L	HBA %	TG mmol/L	TC mmol/L	HDL-C mmol/L	LDL-C mmol/L
			Diabetics			
Basal	10.3^{a}	16.6^{a}	2.73^{a}	7.14^{a}	1.46^{a}	4.43^{a}
WK1	7.8^{b}	14.2^{a}	$1.92^{a,b}$	$5.84^{a,b}$	$1.35^{a,b}$	3.61^{a}
WK2	$8.8^{a,b}$	14.0^{a}	$1.87^{a,b}$	$5.56^{a,b}$	$1.15^{b,c}$	3.56^{a}
WK3	$9.2^{a,b}$	14.0^{a}	1.30^{b}	$6.21^{a,b}$	1.03^{c}	4.58^{a}
SE*	0.9	1.8	0.48	1.00	0.13	0.86
			Non-diabetics			
Basal	4.0^{a}	12.0^{a}	1.71^{a}	4.73^{b}	1.56^{a}	2.38^{a}
WK1	3.9^{a}	11.3^{a}	$1.32^{a,b}$	4.86^{b}	1.25^{b}	3.00^{a}
WK2	4.3^{a}	10.5^{a}	1.19^{b}	4.76^{b}	1.18^{b}	3.04^{a}
WK3	4.4^{a}	10.3^{a}	1.15^{b}	4.97^{b}	$1.29^{a,b}$	3.12^{a}
SE†	0.50	0.93	0.16	0.10	0.10	<0.32

*Values = Group Mean
GLU, serum glucose; HBA, glycosylated hemoglobin (%); TG = serum total triglyceride; TC, serum total cholesterol; HDL-C = serum high density lipoprotein cholesterol; LDL-C = serum low density lipoprotein cholesterol.
Means for either diabetic or nondiabetic groups of subjects within a vertical column differed significantly ($P < 0.05$) unless they shared a common superscript letter.
†Based on pooled variance after correcting for the effect of period and subject.

the self-selected diets were similar among the two groups; and body weights were stable *(Figure 1)*.

A preliminary analysis of dietary records of subjects *(Table 3)* suggests that, apart from the supplement, they consumed, on average, amounts of daily dietary fiber similar to currently accepted values of 11 g for women and 17 g for men in the USA.[14] Presumably, nearly one-third of this was soluble dietary fiber. Further supplementation with 1.7 g soluble and 10.4 g insoluble fiber per day was substantial but elicited few complaints of abdominal distress.

The fiber supplement was effective in altering blood lipids. Serum triglyceride decreased ($P < 0.05$) after 2 weeks of fiber supplementation among nondiabetic subjects; while among the diabetics a trend towards triglyceride decline reached statistical significance 1 week after cessation of the supplement. Total cholesterol tended to decrease during the feeding of the supplement among diabetic but not among the nondiabetic subjects. To our surprise, HDL-C also decreased. We note, however, that several fiber supplements have been reported to reduce or tend to reduce HDL-C after 3 weeks of feeding,[15] while guar gum in crisp bread lowered HDL-C transiently (3 weeks) but not after prolonged feeding.[16] Locust bean gum fed for 16 weeks also decreased HDL-C by 17% in familial hypercholesterdemic subjects.[17] The main finding is that removal of the fiber supplement for 1 week did not alter any of the serum lipid components.

Discussion

The results of the present study suggest the possibility of a persistent effect of dietary fiber in metabolism. The Staub-Traugott Phenomenon[18,19] represents the first indication in the literature of a carry-over effect of dietary complex carbohydrates. This phenomenon has been utilized to explain the observation of improved carbohydrate tolerance to a second meal when it followed a lente carbohydrate meal.[20] This short-term carry-over effect has subsequently been shown[21,22] to occur only with normal or near normal islet beta cell function. The present study was designed to evaluate the possibility of a carry-over effect 1 week after 15 days of dietary fiber supplementation in free-living normal NIDDM. One week after withdrawal of the supplement, carry-over effects were observed for serum triglyceride, which was depressed ($P < 0.05$) from basal levels among both diabetic and nondiabetic subjects, and also for HDL-C, among diabetic subjects.

Effects of the fiber supplement on glycemic control were not simple or clearcut. Among nondiabetic subjects, fasting plasma glucose did not change from week to week; but a trend toward a decreasing fraction of glycosylated hemoglobin (HBA_{1c}) *(Table 3)* suggests that fiber treatment may have reduced the glycemic response to eating. Among all subjects, fasting plasma glucose at wk 1 and tended to remain below the basal level at wk 2 and wk 3. It appears that blood glucose underwent little, if any, rebound toward the basal level during the week after the withdrawal of the fiber supplement.

Although dietary fiber is well recognized as an important food component in diabetic control and management, studies in this area have been mostly focused on postprandial glycemic response.[23–28] Also, most of these studies[29,31] changed other dietary components beside fiber, e.g., the amount and fatty acid composition of fat. A realistic assessment of dietary fiber needs to be studied under meal conditions. Meals are complex in make up. They contain mixtures of fibers with different physico-chemical properties. In the present study the metabolic effect of Fiber Excel, a supplement containing mixtures of water-soluble and bulk-producing complex carbohydrates was studied in free-living NIDDM and nondiabetic subjects, living their normal lifestyles.

To date, fiber research has rarely addressed the practical problem that the sustained feeding of high fiber foods in the treatment and management of diabetes mellitus and related health disorders is frequently accompanied by undesirable gastrointestinal side effects.[32–36] The present study suggests that the metabolic effects of dietary fiber in NIDDM and nondiabetic subjects may persist when fiber intake is briefly reduced.

Triglyceride response to dietary fiber has been shown to be dependent on the available carbohydrate content of the diet of subjects prone to be hyperlipidemic.[15,37–39] While serum TG has often not been affected by dietary fiber,[15,37] the incorporation of generous amounts of plant fiber from ordinary food stuff into the diet of diabetic subjects inhibited the hypertriglyceridemic response to high-carbohydrate diets[38,39] and in particular, decreased the postprandial triglyceride response. In the present study, self-selected diets were lower in fat than is typical for the population of the USA. This factor may help to explain the marked decrease in plasma triglyceride from basal levels at the end of wk 2 or wk 3.

Although total cholesterol did not change significantly in the supplementation phase of the study, mean values among diabetic subjects were 13% below basal levels 1 week after supplementation ended. This could be medically significant in view of the outcome of the Lipid Research Clinic's primary trial study[40,41] that suggested a 2% lowering of cardiovascular risk for every 1% lowering of plasma cholesterol.

The observed persistence of two fiber effects 1 week after the withdrawal of fiber supplementation has implications relating to the possible role of various short-term effects of fiber that have been suspected of being involved in altering blood lipids and blood glucose levels. These effects include decreased gastric emptying rate, digestion of starch, and absorption rate of glucose and other nutrients;[23,24] a reduced glycemic response to a meal and a reduced elevation of serum insulin;[26,27,30,36] binding of sterols and bile acids in the small intestine and their facilitated discharge in feces;[5,39,42–44] altered location of fat absorption in the small intestines and their facilitated discharge in the feces;[45–48] and changes in the size and half-life of chylomicrons in the blood.[49,50] The resistance of blood lipids to change with withdrawal of extra dietary fiber in the present study suggests that some relatively long-term process set off by eating extra fiber appears to be important in the hypolipidemic effect. The results obtained in this study would suggest the need for a larger scale testing of this concept. Data from such studies, if well characterized, would provide a sound basis for a regimental approach to fiber therapy for specific metabolite control. Reductions in daily frequency of fiber supplementation to achieve specific metabolic goals may generate better dietary compliance among patients.

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